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FACTORS INFLUENCING THE MORTALITY OF PERFORATED PEPTIC ULCER

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AS A RULE a surgeon is optimistic: it is well therefore for him to check up on his statistics occasionally.

From 1925 to 1937, inclusive, there were admitted to the Grady Hospital (both White and Colored Divisions) 155 patients with perforated peptic ulcer.

We include in this study all acute perforated gastric and duodenal ulcers, with consequent soiling of the peritoneal cavity, chemical peritonitis and, if untreated, septic peritonitis. Our reports are not complete, due to incomplete records and lack of autopsies.

For some time we have wanted to compare the mortality rate on ruptured peptic ulcers in our municipal hospital with those of hospitals in other cities.

The incidence of ruptured ulcers varies in different cities; it also varies greatly in different years in the same city. It cannot be explained why the admission to our city hospital varies from one patient to twenty-six patients in different years (table 1).

SEX AND AGE

In our series there were three females, which is 2 per cent. This proportion is in accord with the findings in other cities: perforated peptic ulcer is a man's disease.

Our age incidence ranges from 15 years to 72 (table 2).

From the Grady Hospital.

TABLE 1
Incidence by Years

	White	Colored	Total
1925.....	3	0	3
1926.....	1	0	1
1927.....	1	0	1
1928.....	1	0	1
1929.....	6	3	9
1930.....	5	3	8
1931.....	11	3	14
1932.....	7	11	18
1933.....	9	2	11
1934.....	8	7	15
1935.....	18	7	25
1936.....	17	4	21
1937.....	13	13	26
1938.....	2	0	2
<i>Total</i>	102	53	155

TABLE 2
Age and Sex Distribution

<i>White</i>					
Age	Number of Males	Number of Females	Total	Number of Deaths	Per Cent Mortality
15-20	5	0	5	0	0
21-30	29	2	31	9	29
31-40	29	0	29	9	30
41-50	26	0	26	7	27
51-60	8	0	8	4	50
61-70	2	0	2	2	100
71-74	1	1	2	1	50
<i>Total</i>	100	3	103	32	31
<i>Colored</i>					
Age	Number of Males	Number of Females	Total	Number of Deaths	Per Cent Mortality
15-20	4	0	4	1	25
21-30	17	0	17	1	5
31-40	19	0	19	7	37
41-50	8	0	8	3	37
51-60	4	0	4	0	0
61-70	0	0	0	0	0
71-74	0	0	0	0	0
<i>Total</i>	52	0	52	12	23

155 cases. 44 deaths. 28 per cent mortality.

Although there was no patient under 15 in this series, perforated peptic ulcer may occur in infancy. Dr. L. J. Netto, of West Palm Beach, sent us with permission to publish, his records on two such cases. Because of rarity, these cases are reported in abstract:

CASE 1. A white boy, aged 5 weeks, was admitted to the Good Samaritan Hospital, Oct. 2, 1935.

Chief Symptom: Persistent and projectile vomiting.

Present Illness: Since birth this baby had been unable to retain food. He might take a few ounces, retain it a short time and then vomit. Much of the vomiting was projectile in character. There had been no normal bowel movements since birth, the bowels having been emptied only by daily enemas. Distention of the abdomen had been progressive.

Examination: The patient showed a moderate degree of emaciation and a markedly distended abdomen. Other findings were irrelevant.

Laboratory Findings: Red blood count 3,710,000. Hemoglobin 70 per cent. White blood count 12,350. Wassermann negative and urinalysis normal.

Diagnosis: Congenital pyloric stenosis.

Progress: The patient was operated upon the day of admission. Much inflammatory reaction was found around the pylorus and first portion of the duodenum, adhesive bands and exudate leading to a "penetrating ulcer" in the first part of the duodenum.

The patient died October 14. No postmortem permitted.

CASE 2. A colored boy, aged 4 months, was admitted to Pine Ridge Hospital, Oct. 14, 1935.

Chief Symptom: High fever and convulsions.

Present Illness: Three days previously fever had developed. This would rise rapidly to high levels and shortly be followed by repeated series of convulsions. On the day of admission he had been seen by a doctor in his local community at whose office he had had a severe convulsion. On admission at 7:45 p. m. temperature was 102 degrees. Shortly afterward there was another severe convulsion. By midnight the temperature had risen to 104.6.

Examination: The pulse was rapid and regular. Physical examination otherwise was negative except for slight umbilical hernia.

Laboratory Findings: Red blood count 2,280,000. Hemoglobin 50 per cent. White blood count 11,000. Widal, Wassermann and urinalysis all negative.

Progress: On October 17, three days after admission, dark blood appeared in stools. This was accompanied by abdominal distention and apparently pain. Fever and restlessness persisted until death, which occurred on October 19, five days after admission.

Autopsy: Pathologic findings other than those of acute dehydration were limited to the epigastrium. The first portion of the duodenum was bound to the fundus of the gallbladder with fibrinous adhesions and covered by a portion of the omentum. Two oval perforations of the duodenum just distal to the pyloric sphincter were noted; each was filled with a soft recently formed blood clot. From within the perforations were seen surrounded by a slightly



Autopsy specimen of perforated duodenal ulcer. This patient was a negro boy aged 4 months.

Courtesy of Dr. L. J. Netto

thickened and mottled grayish red inflammatory zone. Small bits of dark blood clots were found in the duodenal lumen.

DIAGNOSIS

In the majority of cases of perforated ulcer the diagnosis is easy. The sudden onset of severe abdominal pain with a rigid abdomen is usually sufficient to make one suspect the correct diagnosis, especially if there is an ulcer history as there often is. In approximately 90 per cent of this series the condition was correctly diagnosed. However, other lesions must be eliminated, such as acute appendicitis, acute pancreatitis, ruptured gallbladder and black-widow spider bite. All cases are not typical and the history may be confusing or deceptive as in the following two case reports:

CASE 3. A white man, aged 40, was attending the Proctology Clinic for injection of hemorrhoids. On this particular day he had attended the clinic and after leaving the hospital went across the street and was sitting on a stool at a lunch counter when he was seized with severe abdominal pain and fell to the floor in a state of collapse and shock. He was sent back to the hospital where the clinic surgeon made a tentative diagnosis of mesenteric thrombosis, which probably was justified considering the history. He was put to bed in the ward. The blood count showed moderate leukocytosis which increased in a few hours. The pain became more severe.

Twelve hours later one of us called in consultation decided that a positive diagnosis was impossible, but that he had an acute surgical condition of the abdomen. He was operated on immediately and a perforated duodenal ulcer

was found with chemical peritonitis. The ulcer was sutured over and a local toilet made of the peritoneal cavity. The patient made an uneventful recovery.

It was discovered the next day that he had not had a hemorrhoid injection but merely an examination.

CASE 4. A white man of about 50 had had a hernia for several years which on the day of admission had strangulated. He had considerable abdominal pain. He was admitted to the hospital and without much difficulty the scrotal hernia was reduced. The patient was put to bed in the ward for observation. The pain continued and there was a moderate leukocytosis with rigidity.

One of us was called to see him in consultation twenty-four hours later and was given the above history. On examination the abdomen was tender and moderately rigid. The scrotum was distended, apparently with air: it would empty on pressure but immediately would refill. An x-ray of the abdominal cavity showed marked pneumoperitoneum.

Operation was performed at once. A perforated duodenal ulcer was closed by suture and the abdomen drained. The hernia was repaired at the same time as the patient's condition was unusually good. He made an uneventful recovery.

In case of doubtful diagnosis one may resort to the use of the x-ray to demonstrate pneumoperitoneum high up in the abdomen under the diaphragm, which if found is positive evidence of a perforated viscus (but its absence does not rule out perforated ulcers, as the perforation may be small and it may be plugged).

SITE OF THE ULCER

Boggon, of St. Thomas Hospital, London, states that the site of the ulcer determines to a great extent the mortality rate. He gave three general groups according to location:

1. Ulcers situated in the pyloric and prepyloric regions;
2. Those in the duodenum;
3. Those in the middle or high up on the lesser curvature of the stomach.

The mortality rate in these groups varied greatly, those in the first group, 14.6 per cent; in the second group, 21.6 per cent; and in the last group, 61.9 per cent. One can readily understand the rise in mortality from the prepyloric to duodenal groups, but 61.9 per cent is appalling. In the third group the approach may make the operation more difficult: the incision is most often to the right of the median line which, in a rigid abdomen, accentuates the inaccessibility of the perforation. The chronic induration of these ulcers also tends to a retraction of the gastrohepatic omentum; this makes the stomach less mobile and prevents its being drawn down into the wound. This chronic induration also makes enfolding of the perforation more difficult, and the operator may so traumatize the area as to increase the danger of postoperative chest compli-

cations. For these reasons the mortality is bound to be higher than in perforation in other regions. A transverse abdominal incision would probably help to eliminate these difficulties. Such an incision would be especially advisable if the exact location of the ulcer has been previously determined.

In our series there were eighty-one gastric ulcers and seventy-three duodenal ulcers. One patient had two perforations—gastric and duodenal. In another patient the location of the ulcer was not recorded. The mortality of gastric ulcers was 27 per cent and of duodenal ulcers 24 per cent.

TABLE 3
Location of Ulcer

<i>White</i>					
	Number of Cases	Number of Deaths	Mortality Per Cent		
Gastric	49	15	30		
Duodenal	53	15	28		
Gastric and Duodenal	1	1	100		
Unknown	1	1	100		
<i>Colored</i>					
	Number of Cases	Number of Deaths	Mortality Per Cent	Total	Mortality Per Cent
Gastric	32	8	25	81	27
Duodenal	20	4	20	73	24
Gastric and Duodenal	0	0	0	1	100
Unknown	0	0	0	1	100

MORTALITY

Of the 155 patients in this series 44 died, directly or indirectly from the perforations, giving a mortality rate of 28 per cent. This mortality is too high, especially since we are dealing with a condition which supposedly is easy to diagnose and easy to treat.

In our private practice, which consists mainly of referred patients, the mortality has been 25 per cent. Most of these patients were referred by doctors 60 to 150 miles distant from Atlanta, and arrived twenty-four to forty-eight hours after perforation. Patterson,¹ of Cuthbert, Georgia, reports a series of 35 cases with a mortality of 11 per cent, which is very good. McCreery,² of New York, reported a series of 170 patients with a mortality of 35, or 20.5 per cent. Tilton,³ of New York, reported a series of 52 patients with only one death, a very low mortality of 2 per cent.

The factors which may influence the mortality rate are the length of time between perforation and operation, the patient's

general condition, age, and the type of operation performed (whether conservative or radical), the length of time the patient is kept on the operating table, the drainage employed, the type of anesthetic used and the postoperative treatment given.

Usually the mortality is directly in proportion to the number of hours elapsing between the time of perforation and operation, the best results being obtained when operation occurs within the first six hours after perforation (table 4).

TABLE 4
Time from Perforation to Operation

<i>White</i>			
Hours Elapsed	Number of Cases	Number of Deaths	Mortality Per Cent
1 - 6.....	63	12	19
7 - 12.....	26	12	46
13 - 18.....	6	2	33
18 +	8	6	75
<i>Colored</i>			
Hours Elapsed	Number of Cases	Number of Deaths	Mortality Per Cent
1 - 6.....	29	4	13.7
7 - 12.....	13	2	15
13 - 18.....	1	1	100
18 +	6	4	66

However, we have had cases recover when operation was delayed for two days after the perforation.

We have a fairly good ambulance service at Grady, and in the majority of instances the patient with ruptured ulcer is brought in promptly. Recently we were called to the hospital in consultation to see a patient who had been in the Medical Ward ten days under treatment for ulcer of the stomach. The ulcer perforated at 4 a. m., and it took seven hours to get him to the operating room. It probably would have been better for him had the perforation occurred at home. This patient died on the eighteenth day of chest complications. It is easy, but entirely wrong, to assume that because a patient is in the hospital and under observation he is safe from perforation. He is only safe if the observation process is carried out to the letter. C. F. Vale and D. A. Cameron, of Detroit, called attention to the grave risk of patients succumbing to a perforation while in the hospital. They reported a series of seven patients, all of whom died.

TYPE OF OPERATION

A review of recent literature shows that there is still considerable difference of opinion as to the most advisable type of operation. The operative procedure varies a great deal in the hospitals of America, as compared with those in Europe. In Germany and Russia the tendency is toward partial gastrectomy.

Judine, of Moscow, reports 168 partial gastrectomies for perforation with the remarkably low mortality of 6 per cent. Kreuter from Nuremberg reports 80 cases treated by resection with a mortality of 21.4 per cent, and Augerer, of Innsbruck, reports a mortality of 14 per cent for a series of 92 patients treated similarly.

In some cases a secondary resection must definitely be considered. Of course, the mere suture of a perforation cannot be considered a cure for the ulcer; the patient must receive medical treatment later. In one of our private patients with a perforated gastric ulcer and extensive induration, a second operation was advised, and when it was performed several months later the patient had an inoperable carcinoma of the stomach with metastases to the liver. We believe the gastroscope will prove a great asset in the after treatment of gastric ulcers to determine their progress. In four of our cases perforation occurred more than once. In one of these the recurrent ulcer had become adherent to the liver and the gastric contents had digested a thimble-shaped depression in the liver substance.

In Great Britain, as in America, the feeling is in favor of a less radical procedure. The immediate mortality of gastric resection and the so-called "old case" is not negligible, especially in the hands of inexperienced operators. One of the golden principles of surgery and one which must always be borne in mind is, "A very ill patient must never be subjected to more than he can stand." The main object is to close the perforation and aid the patient to overcome his peritonitis. The most common operation in the English-speaking countries therefore is simple closure of the ulcer, and the omentum is used to reinforce the sutured area.

In any large hospital or clinic where there is a visiting staff as well as a resident staff, such emergencies as ruptured peptic ulcers are necessarily handled by a large group of surgeons; they are too often left to inexperienced hands. In such institutions the results are not always up to standard. However, while the experience of the surgeon who operates is a factor in reducing the mortality, it appears to be less important than the type of operation performed and the length of time the patient is kept on the table. The young and timid operator is less likely to attempt a radical operation than

one more experienced. It must be emphasized that the length of time on the operating table means everything to these patients, and therefore the type of operation is a most important factor in determining the mortality rate.

Occasionally these patients are admitted in a state of shock, with cold clammy skin, weak thready pulse and low blood pressure. Such patients should be given large doses of morphine, stimulants and fluids subcutaneously, with heat applied externally to prepare for surgery. If such measures are neglected these patients may die on the table or from postoperative shock. In cases of this type, when there is the incentive to operate immediately, the judgment of the experienced surgeon is most valuable.

In the majority of the cases in this series a simple suture of the perforation was done, reinforced by the omentum followed by a local toilet of the peritoneal cavity with drainage. In a few cases the ulcer was excised and pyloroplasty done, a longitudinal excision and a transverse closure to prevent stricture of the pylorus. A few cases had a posterior gastroenterostomy.

TABLE 5
Operative Procedures

<i>White</i>			
	Number of Cases	Number of Deaths	Mortality Per Cent
Simple closure	65	19	29
Excision and closure	21	7	33
Gastroenterostomy	5	2	40
Cauterization and closure	2	1	50
Pyloroplasty	2	0	0
Resection	1	1	100
<i>Colored</i>			
	Number of Cases	Number of Deaths	Mortality Per Cent
Simple closure	49	12	24
Excision and closure	3	0	0

The success of a simple suture operation depends upon a localized peritonitis, and upon the patient overcoming the peritonitis which he cannot do unless his general condition is good. Chest infection lowers a patient's vitality and may kill the patient indirectly by giving the peritonitis every opportunity to progress rapidly.

DRAINAGE

The majority of our cases were drained after operation for fear of septic peritonitis. A review of the literature shows that there

is also a difference of opinion as to whether or not the abdomen should be drained after perforation. Some always drain, some drain late cases and some never drain. We will all admit that the stomach contents are not sterile and that septic peritonitis is inevitable in the majority of cases unless the perforation is closed promptly. We will also admit that a certain number of abscesses will form. In our opinion the abdomen should be drained, at least when operation is done after six hours.

TABLE 6
Causes of Death

Generalized peritonitis	21
Pneumonia	7
Subphrenic abscess	6
Died on table.....	3
Intestinal obstruction	2
Hemorrhage—1 cautery, 1 excision.....	2
Duodenal perforation overlooked (autopsy).....	1
Gastric ulcer not closed efficiently (autopsy).....	1
Pulmonary embolus	1
Total.....	44

ANESTHETIC

These patients should never be given an irritating anesthetic such as ether, if it can be avoided, particularly if there is a bronchial irritation present. It is better to use gas with a local novocain infiltration. Chest complications apparently are more common when spinal anesthesia is used. It was noted that in the majority of these cases of perforated ulcer that the patient had a filthy mouth with advanced pyorrhea and in many cases dental caries.

CAUSES OF DEATH

There were three deaths on the operating table. In some cases no autopsy was permitted. In the majority of cases septic peritonitis was present and, in addition, there was an unusually large number of chest complications (table 6).

CONCLUSIONS

The main features influencing the death rate are the length of time between perforation and operation, the risk rising very rapidly after the first six to twelve hours; the age of the patient (above 50 years the danger increases); the location of the ulcer, those high on the lesser curvature being especially dangerous; the anesthetic plays a small part, as does also the length of time of the operation, and the operative procedure, whether conservative or radical.

The length of time before operation should in all cases be reduced to under six hours by early diagnosis and prompt operation. It is our opinion that in the majority of instances a simple suture of the perforation reinforced by the omentum is the operation of choice. In the words of the great John B. Murphy, "Get these patients on the table quick and get them off quicker."

It is our opinion that our mortality of 28 per cent is entirely too high, and that our surgical staff as a whole should cooperate in order to bring about a lower mortality.

REFERENCES

1. Patterson, J. C.: Perforated Peptic Ulcer, *J. M. A. Georgia* 25: 20 (Jan.) 1936.
2. McCreery, J. A.: Perforated Gastric and Duodenal Ulcer, *Ann. Surg.* 107: 350 (March) 1938.
3. Tilton, B. T.: Low Mortality of Early Operation for Perforated Gastric and Duodenal Ulcer, *Am. J. Surg.* 32: 238 (May) 1936.
4. Trout, H. H.: The Treatment of Perforated Peptic Ulcers, *J. A. M. A.* 104: 69 (Jan. 5) 1935.
5. Portis, S. A., and Jaffe, R. H.: A Study of Peptic Ulcer Based on Necropsy Records, *J. A. M. A.* 110: 6 (Jan. 1) 1938.
6. Read, J. C.: Review of One Hundred Cases of Acute Ruptured Peptic Ulcer, *South. Surgeon* 7: 436 (Oct.) 1938.

AN OPERATION FOR THE RELIEF OF EPILEPSY FOLLOWING CERTAIN TRAUMATIC AND INFLAMMATORY LESIONS OF THE BRAIN

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ONE of the most frequent causes of epilepsy is cerebral trauma and, less commonly, inflammatory lesions of the brain. Reference is not made in this presentation (in regard to trauma) to convulsions following depressed fractures over or adjacent to the motor areas of the cerebral cortex or severe contusion and laceration of the cerebral hemispheres; convulsions, in such cases, are due, presumably, to a more or less direct involvement of the motor cortex or the subcortical motor pathways (by gliosis, traction and scarring), from which relief is usually (although not invariably) obtained, by removal of the post-traumatic lesion of the brain.

We are concerned particularly, in this discussion, with the more subtle causes of epilepsy following certain traumatic (and inflammatory) lesions of the brain, especially those cases in which the injury or infection causes complete or almost complete obliteration of the basilar cisternae, which in themselves serve as the only connecting pathway in the circulation and absorption of cerebrospinal fluid. These cisternae lie midway between the ventricular system and the subarachnoid spaces over the cerebral convexities, in which latter region absorption of the fluid takes place into the dural venous sinuses by means of the arachnoidal villi which project into them, according to Spurling¹ and others.

Presumably, if a block in the cerebrospinal fluid circulation occurs in the basilar cisternae as the result of adhesions incident to and subsequent to trauma or infection of the brain, there will result a damming back of fluid (at intervals, at least, in the event that the basilar obstruction is not complete) with the result that convulsions may occur. Furthermore, if a patient with post-traumatic or post-infection convulsions has, in addition, a well-developed internal hydrocephalus, as a result of such a block, it is conceivable that a short-circuiting of the fluid from one or both lateral ventricles to the subarachnoid spaces over the cerebral hemispheres, together with an obliteration of one or both choroid plexuses in the lateral ventricles (the source of most of the fluid), would result in a diminution or possibly complete disappearance of the attacks.

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The following case apparently demonstrates the feasibility of such an operation:

Thirty-one year old shipyard worker with several grand mal seizures a month, beginning two years after severe head trauma. Phenobarbital therapy, dehydration and other measures, ineffective in controlling seizures. Encephalogram (on two occasions) demonstrated enormous internal hydrocephalus with complete absence of air over cerebral cortex and, for the most part, in the basilar cisternae. Creation of stoma between right lateral ventricle and right cerebral subarachnoid space, together with obliteration (by electrocoagulation) of right choroid plexus, resulted in disappearance of all seizures up to twenty-three months after operation, with the aid of no supportive drug therapy.

Elijah B., aged 31, a white shipyard worker, was referred by Dr. T. E. Patterson of Ranson, Virginia, to the service of Dr. D. C. Wilson for investigation of convulsive seizures on Dec. 13, 1937 and discharged improved on Feb. 5, 1938.

He had been well until April 6, 1933* when he had been rendered unconscious by a blow in the right temporal region from an iron pipe wielded by an assailant. He remained unconscious for eight hours; there was slight bleeding from the right ear. He was confined to a hospital in another state for eight weeks thereafter and, at the time of discharge, he was in good condition except for total deafness in the right ear.

He began work in a shipyard, being able to work without ill effects, until Aug. 22, 1935, when he had a generalized convulsion characterized (according to the statements of onlookers) by complete unconsciousness, opisthotonos, generalized clonic movements of the extremities, facial cyanosis, groaning, salivation and tongue biting. The attack lasted about thirty seconds; following the seizure, he felt weak and dizzy and slept for about an hour.

This type of seizure occurred a great many times in the ensuing two years or more, sometimes as frequently as five or six times a day. An encephalogram was done at the time of onset (1935) in another hospital which showed an enormous internal (communicating) hydrocephalus, no air in the subarachnoid spaces over the cerebral convexities, and little or no air in the basilar cisternae. He continued to have seizures after the encephalogram with equal intensity and frequency in spite of phenobarbital therapy and a dehydration regime.

On Jan. 15, 1937, a somewhat different type of seizure developed, in addition to those which began in 1935: he fell to the ground without premonitory aura in a semiconscious state, remained stuporous for an hour or more and was vaguely conscious of people standing nearby. From July 15 to November 29, he experienced five such seizures, the last two of which occurred within four hours of each other and were further characterized by muscular rigidity and twitching. The patient had been taking $1\frac{1}{2}$ grains of phenobarbital four times a day for two years or more before admission to the hospital, during which time the seizures became more frequent than ever.

Examination disclosed an attractive, cooperative individual who was intensely interested in obtaining relief from his convulsions by any means whatever. Neurologic examination demonstrated no evidence of increased intracranial pressure. The fundi were normal and extra-ocular movements were

*The exact dates of this and subsequent significant events in the patient's history are possible due to his extraordinary memory for all important occasions in his life, even to recalling the month and the day of every incident.

full and equal. The left pupil was slightly larger than the right one. There was total deafness in the right ear. The patient was right-handed and there was no aphasia, astereognosis, loss of motor power in any extremity or visual field abnormality. There were no reflex inequalities and no ankle clonus or positive Babinski sign was present. Tests for cerebellar function, including the Romberg test and gait, were normal. The temperature, pulse and respiration were within normal limits; the blood pressure was 130/88.

Urinalysis and blood count were not unusual except for 12,800 white blood cells. The blood and spinal fluid Wassermann reactions were negative. The spinal fluid contained 6 lymphocytes and 30 mg. of protein.

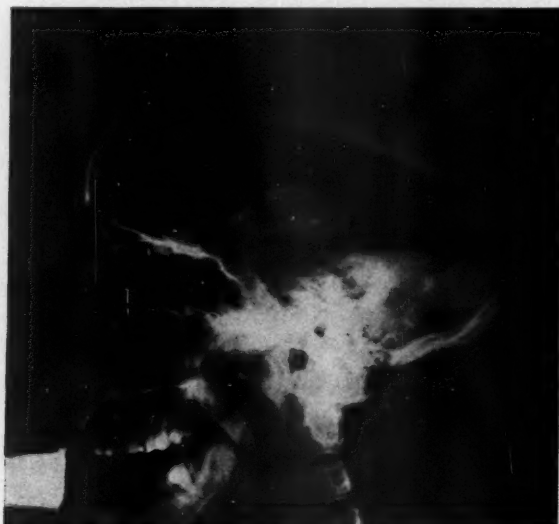


Fig. 1. Lateral view of encephalogram, performed thirty-three days before operation. Enormous internal hydrocephalus is evident: this is of the communicating type as the air was injected into the lumbar subarachnoid space. No air is visible over the cerebral hemispheres and very little is seen in the basilar cisternae except for a moderate amount in the cisterna interpeduncularis (posterior and above the dorsum sellae) and a small amount in the cisterna chiasmatis (arrow). The third ventricle is well shown as is the upper portion of the aqueduct of Sylvius. The block in the basilar cisternae has resulted in internal hydrocephalus and in an obstruction to the further flow of fluid to the cerebral subarachnoid spaces for absorption into the venous sinuses via the arachnoidal villi: a potent cause for convulsions.

On Dec. 14, 1937, the day after admission, he had a convulsion at 6 p. m. while standing beside the bed of a fellow-patient: he fell to the floor and a generalized clonic convulsion with complete unconsciousness ensued. During this seizure, the patient was in an opisthotonoid state and the arms were acutely flexed. The attack lasted about four minutes and was followed by a period of deep sleep for an hour or more, characterized by stertorous respiration and a rapid pulse of poor quality. The following day (December 15) another convulsion occurred at 6 a. m.

On December 16, an encephalogram was performed under avertin-gas anesthesia. The initial pressure in the sitting position was 45 cm. water. Two hundred fifty cubic centimeters of fluid were removed in fractional amounts and replaced by 245 c.c. of air. X-ray films (figs. 1 and 2) demonstrated tremendously dilated lateral ventricles; the third ventricle and the upper portion of the aqueduct of Sylvius were also visible. There was no trace of any air over the cerebral hemispheres and scarcely any in the basilar cisternae, except for a small amount in the cisterna interpeduncularis.

The patient suffered no ill effects from the encephalogram, apart from the usual severe headache which lasted for two or three days.



Fig. 2. Postero-anterior view of encephalogram performed thirty-three days before operation. The symmetrical and enormous dilatation of the lateral ventricles and the third ventricle is again evident. There were no clinical or operative findings suggesting increased intracranial pressure.

At this time, it was explained to the patient that an operation might be of help to him. He was told that, at the time of the severe head injury in 1933, considerable subarachnoid hemorrhage had undoubtedly occurred with resultant marked impairment of the normal cerebrospinal fluid circulation from adhesions, especially along the base of the brain. An attempt would be made, with his permission, to short-circuit the flow of fluid directly from the ventricle to the cerebral subarachnoid spaces, together with excision of the right choroid plexus to diminish the total amount of fluid formed. It was thought that if this reasoning were correct, the periodic blockage of cerebrospinal fluid flow along the base of the brain, due to adhesions in this region, could be avoided with subsidence of the convulsions. He eagerly assented to the operation.

Accordingly, on Jan. 18, 1938, a right temporoparietal bone flap was turned down without undue difficulty, although there was an annoying persistent oozing of blood throughout the operation, especially after the right lateral ventricle was opened, due to the intracranial *hypotension*. The cerebral convolutions were somewhat flattened and slightly yellow in appearance. The dura was not under increased tension and was opened by means of a circular flap with the base upward. A transcortical incision (5 cm.) was made into the right lateral ventricle through the posterior parietal lobe, a cone of cere-

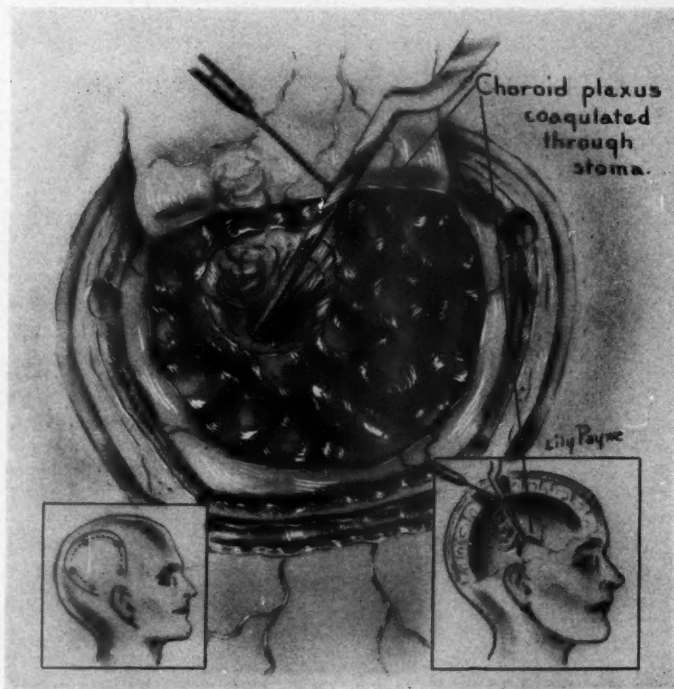


Fig. 3. Artist's drawing of the operation. The cone-like excision of a portion of the right parietal lobe, extending into the lumen of the right lateral ventricle is well shown. Left lower inset demonstrates the location of the bone-flap and the right lower inset shows the electrocoagulation of the choroid plexus being carried out. These procedures accomplish the dual purpose of (1) short-circuiting the flow of cerebrospinal fluid (in part) from the ventricle, avoiding the obstructed basilar cisternae, to the cerebral subarachnoid spaces, thus enhancing absorption into the dural venous sinuses via the arachnoidal villi; and (2) reducing (by about one-half) the total amount of cerebrospinal fluid formed. If convulsions are reduced in frequency and severity (but not abolished) by the operation, the procedure may be repeated on the *opposite* side: the stoma should be smaller to avoid damage to speech centers near this region (in right-handed individuals).

bral tissue being removed with the apex inward toward the ventricle (fig. 3). The choroid plexus in the floor of the right lateral ventricle was completely coagulated with the electrosurgical apparatus but it was not removed.

The diameter of the stoma in the ventricular wall was fully 3.0 cm. The ependymal lining of the ventricle was smooth and glistening and, to all appearances, normal. There was no undue bleeding at any time. On gently retracting the margins of the stoma on several occasions before closure, at least 15 c.c. of ventricular fluid welled up to and over the surface of the right cerebral hemisphere. At the time of closure, the brain fell away for a distance of 4 cm. from the under surface of the dura. The dural flap was completely resutured to the surrounding dura, an extradural drain was inserted (for twenty-four hours) and the bone flap replaced. The scalp was closed in layers by means of interrupted silk sutures and the patient was returned to the ward in excellent condition.

The postoperative course was satisfactory. He was discharged from the hospital eighteen days after operation with instructions to take $1\frac{1}{2}$ grains of phenobarbital three times a day until further notice. At the time of discharge, there was no weakness of the left side of the body, no astereognosis and no hemianopsia.

Follow-Up Notes. The patient has been seen at frequent intervals since operation. No convulsions—grand or petit mal—have occurred at any time in the twenty-three months' period following operation *although all phenobarbital therapy was stopped one year after operation (Jan. 18, 1939).* The last (Dec. 5, 1939) follow-up letter stated that the patient had had no petit or grand mal seizures since the operation twenty-three months previously; he had no headache, vertigo, or other disability and considered himself quite well ("I feel better than I have for years"). When it is recalled that the patient had had, on the average, four severe convulsions every month before operation, completely incapacitating him from all work, it is demonstrated that real improvement has occurred postoperatively to date.

COMMENT

The normal circulation of cerebrospinal fluid proceeds from its chief points of origin in the choroid plexuses of the lateral ventricles, through the foramina of Monro to the third ventricle, and then to the fourth ventricle via the aqueduct of Sylvius. Its mode of exit from the fourth ventricle is by way of the medially placed foramen of Magendie and the two laterally placed foramina of Luschka whence it enters the large cisterna magna of the subarachnoid space. From the cisterna magna the fluid passes in two directions: (1) upward and forward about the base of the brain (fig. 4) to reach the surface of the cerebral hemispheres from which it is ultimately absorbed into the dural venous sinuses (chiefly the superior longitudinal sinus) by means of the arachnoidal villi which project into them; (2) downward in the spinal subarachnoid space over the surface of the spinal cord. Thus the cerebrospinal fluid is in continuous movement, in definite directions, through a highly specialized pathway¹.

If obstruction to the flow of fluid be present in the form of adhesions in the subarachnoid basilar cisternae (fig. 5), subsequent

to trauma and infection therein, or either, cerebrospinal fluid is prevented from reaching the subarachnoid spaces over the cerebral convexities for ultimate absorption. The characteristic roentgenologic (encephalographic) appearance is that of internal (communicating) hydrocephalus, with little or no air over the cerebral hemispheres or in the basilar cisternae. The operation described above

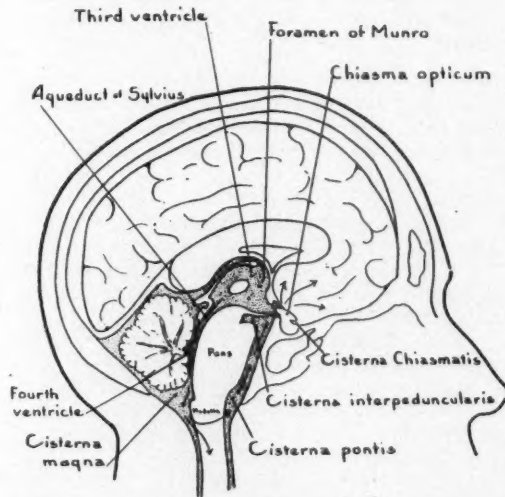


Fig. 4. Artist's sketch of a portion of the *normal* cerebrospinal fluid circulation. Fluid is formed in the lateral ventricles, from which structures it proceeds (arrows) to the basilar cisternae (via the aqueduct of Sylvius and the fourth ventricle) to continue therefrom to the cerebral subarachnoid spaces and ultimate absorption into the venous sinuses through the arachnoidal villi.

has been designed to short-circuit the flow of approximately one-half of the fluid from its site of formation in the right lateral ventricle to the subarachnoid spaces over the right cerebral hemisphere. A certain amount of fluid from the *left* lateral ventricle also probably escapes through the stoma via the third ventricle and the right lateral ventricle, rather than proceeding down the aqueduct of Sylvius to the fourth ventricle.

The rationale of the operation is dependent on two conditions:

1. Are the subarachnoid spaces over the cerebral hemisphere *patent** in such a case to permit of ingress of fluid directly from the ventricle through a cerebral stoma? 2. Does the stoma remain *per-*

*It is recommended that the excision of the cortex be made (for the most part) with an *ordinary scalpel* rather than with an electrosurgical knife as the subarachnoid space would be likely to become sealed off if the latter instrument were used.

manently open to facilitate the new circulation? These questions could be answered, at least in part, by an encephalogram at the present time, but we have been unable to bring ourselves to the point of doing this, as the patient has continued to do well and would therefore not be benefited himself by the procedure.

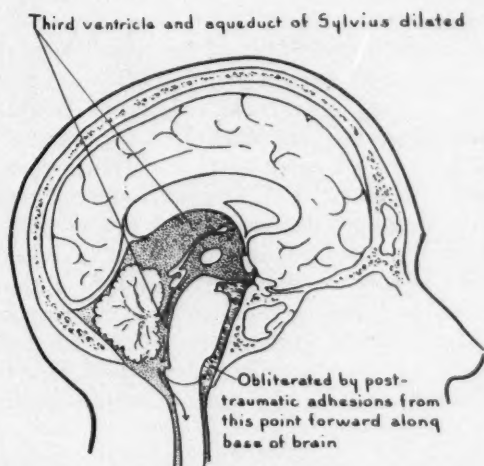


Fig. 5. Artist's sketch to demonstrate the essential lesion in the patient whose case is described in the text. The post-traumatic adhesions obstruct the further flow of fluid from the fourth ventricle to the cerebral subarachnoid spaces. The ventricular system is greatly dilated (compare with fig. 4). The operation, consisting of (1) "short-circuiting" the flow of fluid from the dilated ventricular system to the cerebral subarachnoid spaces without the necessity of having to traverse the obstructed basilar cisternae and (2) electrosurgical coagulation of the right choroid plexus, has resulted in disappearance of convulsive seizures to date (twenty-three months after operation).

It might be argued that such a basilar obstruction to the flow of cerebrospinal fluid should result in more or less *continuous convulsions*, but it is no more reasonable to suppose this than it would be to state that a cortical scar would do likewise (i.e., cause *continuous convulsions*). Probably constant variability in brain volume accounts for the periodic damming back of fluid and resultant *intermittent convulsions*.

Dandy² has devised an operation for congenital obstructive (non-communicating) hydrocephalus in infants in which an opening is made between the floor of the third ventricle and the cisterna interpeduncularis. He emphasized, however, that for the operation to be successful, not only must the cisterna interpeduncularis

be patent but also the subarachnoid spaces over the cerebral hemispheres. The same reasoning applies to the operation described in this paper for the relief of epilepsy due to adhesive obliteration of the basilar cisternae.

It is well known that the use of encephalography in the diagnosis of the nature of the lesion in patients with epilepsy, not infrequently results in marked subsidence or complete remission of the convulsions for an indefinite period of time. Davidoff and Dyke³ quoted Bingel (1922) who believed that the beneficial results are mechanical, namely, the breaking up of adhesions. Gardner⁴ likewise reported (1929) therapeutic effects in fourteen cases of epilepsy following encephalography. In 1921, Sharp⁵ utilized the injection of a gas (oxygen or air) into the cerebrospinal fluid spaces as a therapeutic measure in the treatment of meningitis for the purpose of breaking up adhesions. If the cerebrospinal fluid circulation is enhanced (at least temporarily) by air insufflation alone, it is reasonable to suppose that the creation of a stoma uniting a lateral ventricle and the cerebral subarachnoid spaces, together with excision of a fluid-forming organ (choroid plexus) in that ventricle, would be even more beneficial to a cerebrospinal fluid circulation seriously impaired by obstruction in the basilar cisternae.

SUMMARY

An operation is described that has been devised for the relief of epilepsy which follows certain traumatic or inflammatory lesions of the brain resulting in obliteration of the basilar cisternae. The requirements for success in the operation are (1) that a definite internal (communicating) hydrocephalus be present (as demonstrated by encephalography) with (2) little or no air in the subarachnoid spaces overlying the cerebral hemispheres or in the basilar cisternae. The operation consists of a transcortical incision and large stoma formation into the lateral ventricle through a relatively unimportant portion of the less dominant cerebral hemisphere, together with excision of the choroid plexus in that ventricle; this results in a short-circuiting of the fluid around the obstructed basilar cisternae and a reduction in the total amount of fluid formed.

In the patient in whom this operation was performed, convulsions have not recurred up to twenty-three months after operation even after phenobarbital and other anti-convulsive drugs were discontinued for a period of eleven months to date, although the patient was having several severe convulsions every month before operation, in spite of dehydration and phenobarbital therapy.

One sees occasionally such an encephalographic picture in epileptic patients either post-traumatically or after an inflammatory lesion of the brain. In view of the favorable results obtained in the case reported herein, it is urged that further use should be made of the operative procedure described in an effort to combat the devastating effects of convulsive disorders.

REFERENCES

1. Spurling, R. G.: Practical Neurological Diagnosis. Springfield and Baltimore: Charles C Thomas, Publisher, 1930, pp. 154 and 155.
2. Dandy, W. E.: Practice of Surgery (Dean Lewis). Vol. XII, pp. 247-252, 1932. W. F. Prior Co., Inc., Hagerstown, Md.
3. Davidoff, L. M., and Dyke, C. G.: The Normal Encephalogram, Philadelphia, Lea & Febiger, 1937, p. 63.
4. Gardner, W. J.: The Therapeutic Effects of Encephalography. Pennsylvania M. J. 33: 126, 1929.
5. Sharp, E. A.: Artificial Pneumorrhachis in the Treatment of Acute Infections of the Meninges, Arch. Neurol. & Psychiat. 6: 669, 1921.

FACTORS IN THE MORTALITY OF THYROID DISEASE IN A NON-ENDEMIC AREA

An Analysis of 817 Consecutive Surgical Cases and 103 Consecutive Surgical and Nonsurgical Deaths, With a Note on the Value of the Quick Test of Liver Function in the Estimation of Hepatic Damage

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New Orleans

IT IS generally recognized that the mortality of thyroid disease tends to be excessive in a non-endemic area because, as we have previously pointed out¹⁻³, any disease is most a problem where it is least a problem. Lahey's⁴ mortality of 0.85 per cent in 15,200 thyroid operations, Dinsmore and Crile's⁵ mortality of 1.29 per cent for 10,111 consecutive operations for hyperthyroidism, are to be compared with the dishearteningly different statistics in a series of cases many times smaller from this community.

Public health surveys have shown that in certain scattered areas the incidence of goiter is as high in Louisiana as anywhere in the world, but at that, for all practical purposes this is a non-endemic area. Through the courtesy of Dr. J. M. Batchelor⁶, Superintendent of Public Health in New Orleans, I have been supplied with the figures for the city, and a comparison with national rates furnishes little ground for complacency (table 1). Furthermore, if the present trend continues, estimates are that the peak figures for toxic disease in 1935, 1936, and 1938 are likely to be approximated in the current year.

The inevitable conclusion is that while Lahey and Crile have been operating on their thousands with extraordinarily few fatalities, we, with our limited opportunities, have been, proportionately, slaying our ten thousands. It must not be forgotten, too, that statistics quite as good as those published by the Lahey and Crile Clinics are being reported by individual surgeons elsewhere, Heyd in New York, the Bartletts in St. Louis, DeCourcy in Cincinnati, Richter in Chicago, and many others.

From Jan. 1, 1927, to July 1, 1938, 952 surgical cases of thyroid disease were handled at Charity Hospital of Louisiana with 50 deaths, 5.3 per cent. I do not have a definite breakdown of the figures for the last year of that period, and my remarks will therefore be based upon the 817 cases with 44 deaths which occurred prior to July 1, 1937 (table 2).

The cases reported are from Charity Hospital of Louisiana at New Orleans. The studies on the Quick test were made during the author's connection as Assistant Professor of Surgery with the School of Medicine of Louisiana State University.

I also have for comparison with the 284 deaths which occurred in New Orleans from Jan. 1, 1927, to Mar. 15, 1939, a detailed analysis of the 103 medical and surgical deaths from thyroid disease which occurred in Charity Hospital during that same period (table 3). These comparative figures show very clearly that not even half of the thyroid deaths in this community during this period occurred in the large public hospital in which, for various reasons, one might logically expect to find most of them. It can quite fairly be said, therefore, that the statistics of this institution furnish a not unfair cross section of what is happening in a city in which, because thyroid disease is non-endemic, its mortality is excessively high.

One clue to the high death rate immediately presents itself. The excellent results reported in large series of cases in endemic areas are achieved by very small groups of surgeons, not more than three or four at most, operating with experienced teams of assistants, anesthesiologists and nurses, all of whom are in daily contact with thyroid disease. At Charity Hospital—and in the very nature of things the situation can be no different at the private hospitals of the city—even the surgeons who do the most work have very limited opportunities for studying thyroid disease. The 817 surgical cases reported in this paper were handled by 65 surgeons. One of them, incidentally without a death, performed 88 operations, and another 61. But at the other end of the list six surgeons operated on two patients each, and 14 surgeons on one each. One cannot learn a great deal about one of the most treacherous diseases in the world from one case, or even from 88.

THYROID DISEASE IN THE NEGRO

In the 817 cases under consideration (table 2) the mortality for toxic thyroid disease was 9.35 per cent, and for nontoxic disease 2.37 per cent. A striking disproportion is noted in toxic disease between the white and negro mortalities (6.93 and 12.58 per cent respectively), the male and female mortalities (20.53 and 7.93 per cent respectively), and the white male and negro male mortalities (13.04 and 33.3 per cent respectively) (table 4).

The abnormally high death rate of toxic thyroid disease in the negro is an important consideration in a city whose population is approximately 28 per cent colored, and in a hospital in which, year in and year out, the negro admissions approximate 45 per cent of the total number. No explanation is entirely satisfactory. The disease is more infrequent in the negro than in the white subject, but it is by no means rare. The negro may be beginning to lose his native placidity in the strain of modern life, and may, perhaps, have a more inherently serious type of disease than the white man. Cer-

tainly he has a more unfavorable domestic environment. Certainly he tends to delay unduly in seeking medical consultation. Perhaps thyroid disease develops in the race with peculiar intensity, as certain other diseases seem to develop when the native immunity to them is lost. The most reasonable explanation, as we shall point out later, is a long duration of toxicity without treatment, but that explanation does not apply particularly to the astonishingly high negro male mortality, which remains beyond explanation.

NONSURGICAL TOXIC DEATHS

At Charity Hospital—the broken down figures for the whole city are unfortunately not immediately available—89 of the 103 deaths were toxic and 14 nontoxic (table 3). Of the 89 toxic deaths, 40 were surgical and 49 nonsurgical and the facile conclusion that we are doing good surgery, or that we are selecting our surgical cases wisely, will not explain the discrepancy. The yearly variations are inexplicable. From 1927 to 1933 there were 17 surgical and 9 non-surgical deaths. From 1934 to date there have been 23 surgical and 40 non-surgical deaths. In 1938 there were six surgical and 12 non-surgical deaths. So far this year there have been three non-surgical deaths, but none following surgery.

Some of the non-surgical deaths occurred in patients who came to the hospital exceedingly ill and died within a few days, one within 14 hours. A few occurred in patients who had refused surgery. But most of them occurred in patients who had been treated medically over long periods of time, or were under medical treatment, or, to judge from the records, were not being treated at all.

In such a discussion the physical difficulties which have prevailed at Charity Hospital since the demolition of the old buildings in November, 1936, cannot be overlooked. I have personally observed the unfavorable influence of the unavoidable noise and confusion incident to the construction of the new hospital upon four of these fatal cases, and I find notes to the same effect in other records which I have examined. Several times, against all precedent, toxic patients were dismissed to rest in bed at home, with the idea that their domestic environment, however unfavorable, could not possibly be worse for them than the overcrowded negro wards. On one occasion I found an intensely toxic negro patient of my own—she appears in this series of fatalities—in bed with another patient who had had a colostomy for intestinal malignancy and who was then well on her way to death. It will be interesting to see whether the more propitious physical circumstances of the new hospital will alter the disproportion between surgical and non-surgical thyroid deaths. On the other hand, although environment may be invoked to explain the

12 non-surgical deaths which occurred in 1938, it certainly does not explain the 11 which occurred in 1935.

The one non-surgical death in the non-toxic group occurred in a patient who literally strangled on her huge nodular goiter a day or two before the operation was to take place which she had been refusing for months.

THYROID CRISIS

Twenty-three of the 40 surgical deaths were due to crisis (17 diffuse and 6 nodular), as were 33 of the 49 non-surgical deaths (20 diffuse and 13 nodular). This is a not unexpected proportion. Toxic thyroid patients do not bear the strain of daily life very well, and when they are treated by medical measures over long periods of time, they stand literally in jeopardy every hour.

Some of these patients evidenced their toxicity for the first time following emotional strain or psychic trauma. A minor illness, an accident such as a burn, a fracture or a sprain, or a slight infection touched off the fuse of toxicity in others. Lahey notes that even an abscessed tooth can throw a toxic patient into a violent thyroid storm, and the minor infections and colds which occurred in six of these fatal cases unquestionably played an important part in the outcome. One patient, who recovered, developed tonsillitis as she was being prepared for her second lobectomy, and almost lost her life as a result, which proves that intercurrent illness may occur and a serious crisis ensue even when surgery is contemplated, as it was in some of these fatal cases. When such a situation comes to pass under medical management, it places a heavy responsibility upon the internist who has deferred or has not considered surgical therapy.

Bayley and Ransom⁷, Plummer and Mayo⁸, Forbes⁹, Lockwood¹⁰ and others have pointed out, as we have, the evil effect of non-thyroid surgery in toxic thyroid patients. In this group of fatal cases one patient had had a hysterectomy a few weeks before she was admitted with toxic symptoms. One patient had a number of teeth extracted after admission. Another had several teeth extracted after admission, and had other teeth extracted and a gastrointestinal x-ray examination a few days later. Two weeks later she fell out of bed twice, and twenty-four hours later she died in crisis. Still another patient died shortly after returning from a metabolic rate estimation, thus furnishing a perfect illustration of Bayley's¹¹ warning that at certain times even necessary diagnostic procedures should not be done on intensely toxic patients.

Thirty-eight of the 56 deaths from crisis at Charity Hospital (14 surgical and 24 non-surgical), 68 per cent of the total, occurred in the six month period May through October, for most of which

the weather in this community is warm or very hot. I do not find this fact particularly impressive. It is generally known that toxic subjects do not endure hot weather well, and I personally agree with Wilensky¹², that in a locality in which temperate or hot weather is the rule the year round, the heat and humidity of summer do not affect sick patients as they do in colder climates.

The Charity Hospital admissions, for various reasons, are much heavier during the summer months, and the negro admissions are particularly heavy. Negroes, by the way, prefer hot to cold weather. Because there are a larger number of thyroid patients in the hospital during the summer than the winter, there are a larger number of thyroid operations, and, as a result, a larger number of surgical deaths. From 1934 through 1938, for instance, 62 per cent of the thyroid operations on the Louisiana State University School of Medicine services were performed between May and October, during which period, as we have said, 68 per cent of all the crises occurred on all the hospital services.

If the individual cases of crisis are analyzed, other factors than heat are readily apparent. A highly toxic negro woman, for instance, 37 years of age, was ambulatory until she went into crisis on the sixtieth day after admission; she seems to have had no systematic treatment. A white woman, 27 years old, developed diarrhea on the fourteenth day after admission, received Lugol's solution for the first time three days later, developed auricular fibrillation the next day, and died in crisis on the succeeding day. These patients—and others could be mentioned—developed their crises at the height of summer, but hot weather could scarcely be invoked to explain their deaths.

CARDIAC AND OTHER CAUSES OF DEATH

Seven of the surgical and 12 of the non-surgical deaths were classed as cardiac. Lahey's¹³ theory that the entity generally called "the thyroid heart" does not exist is undoubtedly correct, though it is equally true that long-continued toxicity, of which tachycardia is always the major symptom, will eventually wear down the stoutest heart, let alone the one in which disease already exists. The implications of that fact are found in Hertzler's¹⁴ unqualified statement that all thyroid patients who are not operated on and who live long enough will eventually die cardiac deaths, and Lahey's excellent results with surgery on thyrocardiacs clearly indicate the remedy.

Other causes of death in these toxic cases, such as pneumonia, bronchitis, embolism, and similar causes need no special discussion. One patient died of meningitis after a decompression operation for progressive exophthalmos a year after her second lobectomy, and

another of streptococcic sore throat fifty days after subtotal thyroidectomy.

Three patients died on the table, and a number of others, who died later, had respiratory difficulties during operation. Bartlett¹⁵ contends that patients who exhibit such difficulties during induction of anesthesia, as the result of the withdrawal of oxygen, are not likely to endure the greater withdrawal of the later stages, and for their own sakes should be operated on another day. The use of the Bartlett index of respiratory stability (duration of voluntary apnea) will designate most of these patients before they reach the operating room; I have personally found it a very simple and useful index of toxicity and a simple and accurate test of the fitness of the patient for surgery.

CRITERIA OF ADEQUATE TREATMENT

A careful study of these charts suggests that 34 of the 89 toxic patients who died (13 surgical and 21 non-surgical) did not have adequate treatment. Excluded from consideration are the half dozen who died within 14 to 48 hours after admission, though perhaps, if the full gravity of their condition had been realized, some of them, at least, might have been saved. In the other cases, however, necessary measures were omitted or applied unwisely, and the use of Lugol's solution was particularly unreasonable.

Sixteen patients (six surgical and 10 non-surgical) had had iodine for longer or shorter periods of time before admission on the advice of their physicians, or on the advice of their friends, or on their own initiative. Whether one accepts the iodine-fast theory of the Crile¹⁶ school or the theory of Means¹⁷ that iodine therapy is not harmful per se, but merely does no lasting good, it does do harm in one sense: It so beclouds the issues that the physician is often deceived as to the true state of the patient's disease.

Even at the present time there is still a surprising unevenness in the use of iodine. It was used preoperatively in 36 of the 40 surgical cases in this series, for periods varying from 4 to 27 days, and often without apparent reason was withdrawn and then given again. It was used in 21 of the 49 non-surgical cases, though whether therapeutically or as a prelude to possible surgery is not always clear. There was no differentiation between diffuse and nodular toxic goiter in its use, which most surgeons now believe is correct.

Lerman¹⁸ has called attention to the grave prognosis offered by a group of toxic patients who respond badly or not at all to lugolization. In his report he shows a mortality of 1.1 per cent for 706 patients who responded well to iodine, against a mortality of 25

per cent in 25 patients who responded badly. Most of the individuals in the latter group were over 50 years of age, had nodular goiters with some form of cardiac complication, and a relatively low basal metabolic rate. In our 89 fatal toxic cases we found a poor response or no response to iodine in 23 adequately prepared patients, 12 of whom were submitted to surgery. These patients do not entirely fit Lerman's specifications, but it is striking to note, in view of our previous remarks, that 14 of them were negroes, that 9 were males, and that 4 of the nine were negro males.

INACCURATE ESTIMATE OF TOXICITY

A case history might be quoted at this point which excellently illustrates many of the considerations we have been discussing.

A negro woman, 40 years of age, had a clearcut history of uterine fibroids and pelvic inflammatory disease, the latter of which seemed to be in acute exacerbation when she was admitted. Twelve days later she expelled a degenerating submucous fibroid. When her fever still continued, medical consultation was requested. The consultant, who had had a large experience with thyroid disease in an endemic area, and whose attention was not primarily on the pelvic condition, suspected hyperthyroidism. With it in mind, he was able to elicit a perfect history, including an exciting psychic trauma. Toxicity readily explained the recent loss of 30 to 40 pounds, the muscular weakness, the palpitation, the recent anorexia, and the purposeless motions. Only exophthalmos was missing from the classic picture. A basal metabolic rate reading of plus 61 further confirmed the diagnosis, as did the rapid response to Lugol's solution.

The internist issued an urgent warning as to the patient's extreme toxicity and the danger of other surgery until the hyperthyroidism had been corrected. She was prepared for thyroidectomy on the medical ward, and when she was transferred to surgery 16 days later her general condition was excellent and her basal metabolic rate reading was plus 9. A Quick test, the first done, showed a liver function 77 per cent of normal.

For some reason iodine was discontinued for two days on the surgical ward, then was resumed in massive doses for the remaining five days before operation. The patient went to the operating room with a pulse of 100. She died in violent storm 12 hours after subtotal thyroidectomy.

There are many valuable lessons to be derived from this history. The diagnosis of hyperthyroidism was missed for more than two weeks because all the attention, not unreasonably, was centered on the pelvic condition. The intensity of the toxicity was not realized, in spite of the internist's warning, because the patient was not seen by a surgeon until it had been greatly reduced by the use of iodine and other therapy; she was therefore given no glucose or decholin before operation. The Quick test, run for the first time after preparation on the medical ward, was completely misleading, though the error lay in the human factor and not in the test itself. It did

no harm, however, because no attention was paid to it except by the man who ran it. Finally, the surgeon who operated saw the patient for the first time on the table and was deceived by her apparently excellent condition into doing too much surgery. Several other non-surgical deaths occurred on surgical wards during the course of preoperative preparation because the degree of toxicity was underestimated and the patients went into crises under the very eyes of their surgeons.

The toxicity of many patients in this series should have been easy to estimate. Ten had a history of diarrhea or developed it in the hospital. Eight had a history of vomiting, or began to vomit while under observation. Two vomited and had diarrhea at the same time. Fifty-one had suffered a marked weight loss, in many instances from 30 to 51 pounds. One negro woman had lost 92 pounds. Exophthalmos was noted in 42 patients, was progressive under observation in several instances, and in one instance developed in the hospital. Four patients were jaundiced or had been jaundiced; one had an icteric index of 50. Fifteen had or had had a psychosis, or were irrational under observation. In three of the surgical and seven of the non-surgical cases the goiters were substernal. All these symptoms and signs were in addition to the extreme nervousness, restlessness and emotional instability which many of these patients exhibited.

OTHER POSSIBLE FACTORS OF MORTALITY

In 25 cases the basal metabolic rate reading on admission rose in hospital under treatment, or lack of it, and in other cases the rate did not fall at all. Unusual importance can be attached to an elevated rate in a community like New Orleans, where, as Eaton¹⁹ has shown by a study of 160 normal individuals, the rates are low by any of the four commonly used standards. Hyperthyroidism can easily be overlooked, furthermore, if an elevated rate is regarded as necessary for the diagnosis. Lahey²⁰ has pointed this out in his studies on apathetic hyperthyroidism, and Gordon and Graham²¹ have shown that even in an endemic area hyperthyroidism can occur with a minus basal metabolic reading.

Seven of these patients had positive Wassermann reactions, and seven others had formerly had positive reactions. Two of the non-toxic patients who died also had positive reactions. Whether syphilis and its complications played any part in the fatal outcome of these cases is not clear.

Crile and Crile²² have pointed out the importance of advanced age as a factor in thyroid mortality. It did not seem particularly significant in the fatal cases under consideration except that two-

thirds of the patients who developed spontaneous crises were over 40 years of age. This fact seems to support the idea that spontaneous crisis is more likely to occur in older persons, when, unfortunately, the premonitory signs are less distinct, so that the condition may be fully developed before the physician realizes what is happening.

THE RISKS OF LONG-CONTINUING TOXICITY

The patients with whom we deal at Charity Hospital have an unfortunate tendency toward ignoring even large goiters, just as colored women tend to ignore even large fibroid tumors until pain

TABLE 1
DEATH RATES OF THYROID DISEASE PER 100,000 POPULATION

	1933	1934	1935	1936	1937	1938
Toxic						
United States	2.7	2.8	2.8	3.0	2.9	
New Orleans	2.874	3.030	4.780	3.732	2.519	4.206
Non-Toxic						
United States	0.2	0.2	0.2	0.2	0.2	
New Orleans	1.232	0.404	1.593	1.571	1.162	1.338

TABLE 2
INCIDENCE AND MORTALITY OF SURGICAL THYROID DISEASE
AT CHARITY HOSPITAL IN NEW ORLEANS

January 1, 1927 — July 1, 1937			
	CASES	DEATHS	PERCENTAGE
Total	817	44	5.4
Non-toxic	464	11	2.37
Toxic	353	33	9.35
White	414	16	3.86
Negro	403	28	6.94
Male	93	14	15.0
Female	724	30	4.16

or bleeding directs their attention to them. It was impossible, therefore, to determine accurately the duration of the symptoms or of the goiter in most of the toxic cases. It is interesting to note, however, that 17 patients stated positively that they had had their goiters longer than five years, and that 16 others had carried them from one to five years. Pemberton²³ has reported a series of cases in which the duration of illness in the patients who recovered averaged 17.7 months, against an average duration of 28.09 months in the patients who died, and there seems no doubt that the duration of the toxicity plays a dominant part in the mortality of thyroid disease.

Hertzler¹⁴ has advanced the idea that all thyroid disease is one continuous disease process, and has said, further, that even a simple non-toxic goiter is never truly innocent. If one accepts those premises, then one must also accept the conclusion that many of the patients in this series had been suffering from latent if not from active toxicity for long periods of time. The remedy is equally clear, surgery for thyroid disease preferably before it becomes toxic, certainly immediately after toxic manifestations have appeared.

THE MORTALITY OF NON-TOXIC THYROID DISEASE

The mortality of non-toxic thyroid disease in this community (tables 1, 2) cannot be explained on the basis of the patient's condition, the unpropitious circumstances now existent in the hospital, or the heat of summer. Something else is needed to explain the 2.37 per cent mortality in 464 non-toxic thyroids, and to explain a local death rate that in some years is 100 to 800 per cent higher than for the whole country.

It is true that in the 103 fatalities 11 of the 13 surgical deaths in the non-toxic group occurred in negroes, and five of the 11 in negro males, thus carrying out the trend we have noticed in toxic disease. Twelve patients were 40 years of age or older. Two had carried their goiters for more than two and nine for more than five years. Two were obese. Ten had mechanical symptoms, sometimes very marked. Three glands were substernal. Five patients had coexistent cardiac disease and one had diabetes. One had a number of teeth extracted shortly after admission, and two others required incision and drainage for intercurrent infections before thyroidectomy. Three were operated on under ether, which is not the best anesthetic for any sort of thyroid surgery. One bled considerably at operation and three had respiratory difficulties, which suggests the wisdom of using Bartlett's test of respiratory stability even in non-toxic patients.

How important any of these facts and findings are it is not possible to say. It is significant, however, that most of the surgical deaths in non-toxic disease were due to causes usually considered "preventable errors," chiefly hemorrhage, shock, and respiratory depression.

THE LIVER FACTOR IN THYROID DISEASE AS ESTIMATED BY THE QUICK TEST OF LIVER FUNCTION

So much evidence now exists as to the importance of the liver factor in toxic thyroid disease, and the dominant part it plays in thyroid crisis, that no extended discussion of it is needed at this time. Its existence, which can be established by experimental, clin-

ical, and pathologic evidence,²⁴⁻²⁸ is an impressive contribution to the now generally accepted idea that toxic thyroid patients should be treated by surgery before their visceral state becomes irreversible or before they die from spontaneous crisis, if operation be deferred too long.

Necropsy was performed in 23 of these 103 fatal cases. In three the gross and microscopic liver findings were negative. In two cases no microscopic study of liver tissue was made. But in all of the remaining 18 cases the liver showed some involvement: toxic hepatitis and cirrhotic changes in one case each, congestive changes in two, degenerative changes in two, and fatty infiltration in twelve. In view of the emphasis we have placed upon the possible latent toxicity of long-continuing goiters, it is significant that fatty infiltrative changes were observed in the liver of a patient with a non-toxic nodular goiter which she had carried for at least 11 years.

TABLE 3
COMPARISON OF THYROID DEATHS IN CHARITY HOSPITAL AND IN
NEW ORLEANS

January 1, 1927 — March 15, 1939		
	CHARITY HOSPITAL	NEW ORLEANS
Total	103	284
Toxic	89	219
Non-toxic	14	65
White	36	193
Negro	67	91
Male	27	46
Female	76	238

These findings correspond more or less with the findings reported by others²⁴⁻²⁶ who are interested in this phase of thyroid disease. They are supported by our findings in the Quick^{29, 30} hippuric acid liver function test, which show decreased values for both toxic and non-toxic patients (table 5). On the other hand, control patients, who were admitted for simple appendectomy or hernioplasty, showed no such preoperative impairment of liver function.

The Quick test has proved a most satisfactory method of studying thyroid patients, and I was gratified to hear Cattell³¹ of the Lahey Clinic, in a recent lecture in New Orleans, give his testimony to this effect. The Lahey group³² have found, as we have, that when this test is used serially, it indicates with a high degree of accuracy the condition of thyroid patients when they are first seen, their response to preparation, and, in combination with other observations, chiefly clinical, the optimum time for operation and the amount of surgery which can safely be done.

The Quick test was used one or more times in 11 of the 103 fatal cases under discussion. It will be noted from the abstracts which follow that the values on the first test ranged from 92.6 per cent of normal to 29.7 per cent of normal. A patient whose liver function was almost normal on admission (case 1) died of tuberculous meningitis; her toxicity was markedly increased before death, but the initial value is undoubtedly correct. The very low value of 29.7 per cent of normal in another case (case 11) is undoubtedly correct also. This patient was very toxic on admission, was refractory to every attempt at preparation for surgery, and finally died in violent crisis.

CASE REPORTS

CASE 1. A negro woman, 40 years of age, with a toxic nodular goiter, developed tuberculous meningitis ten days after admission to the surgical ward, and died a few days later with a marked exacerbation of toxicity. The initial Quick test of liver function was 92.6 per cent of normal.

TABLE 4
DISTRIBUTION OF TOXIC THYROID DISEASE
AT CHARITY HOSPITAL IN NEW ORLEANS

January 1, 1927 — July 1, 1937			
	CASES	DEATHS	PERCENTAGE
Total	353	33	9.35
White	202	14	6.93
Negro	151	19	12.58
Male	38	8	20.53
Female	315	25	7.93
White male	23	3	13.04
Negro male	15	5	33.3
White female	179	11	6.14
Negro female	136	14	10.3

CASE 2. A white woman, 45 years of age, with a toxic nodular goiter and cardiac complications, was admitted vomiting. She continued to vomit for 48 hours, and developed a diarrhea which was difficult to control. Five weeks after admission she developed a psychosis and refused food. She received no iodine until two days before death, which was due to crisis. The Quick test 19 days after admission, and after intensive glucose therapy, was 81.3 per cent of normal.

CASE 3. A negro woman, 40 years of age, with a toxic diffuse goiter, was prepared on the medical ward and died in storm after a subtotal thyroidectomy by a surgeon who saw her for the first time on the operating table. The detailed history of this case appears in the text. The Quick test, after preparation, revealed a liver function 75.6 per cent of normal.

CASE 4. A negro girl, six years of age, with a toxic diffuse goiter, was carried safely through two lobectomies in spite of intense toxicity. She died a year after the second, following a decompression operation for progressive exophthalmos. The Quick test, one month after her first admission and after

intensive preoperative preparation, showed 71.5 per cent of normal function. Serial tests were done before and after each lobectomy, as well as in the interim, and the results showed definite correlation with her clinical improvement and regression.

CASE 5. A white man, 58 years of age, had a toxic diffuse goiter with repeated heart failure. Lobectomy was done after intensive preparation, and 12 hours later an embolus formed in the femoral artery. He refused amputation for 12 days, and when he finally consented to it, the leg was gangrenous almost to the knee. He died of cardiac failure 13 hours after the operation. The Quick test shortly after admission was 70.7 per cent of normal, and serial tests showed definite correlation with his clinical improvement.

TABLE 5
INITIAL VALUES (IN TERMS OF NORMAL) FOR THE QUICK HIPPURIC ACID
TEST OF LIVER FUNCTION IN THYROID DISEASE

TYPE	FIRST SERIES	SECOND SERIES
Diffuse	83.0	84.6
Toxic diffuse	58.0	54.8
Nodular	50.4	57.7
Toxic nodular	78.8	74.7
Control*	100.0	

*Patients admitted for elective appendectomy and hernioplasty.

CASE 6. A negro woman, 36 years of age, with a toxic nodular goiter, was prepared for operation with great difficulty because she was so much disturbed by the noise and confusion incident to the construction of the new hospital. She died suddenly, without ascertainable cause, three hours after subtotal thyroidectomy. Her temperature, pulse, respiratory rate and blood pressure were within normal range a few minutes before death, and there were no clinical signs of any impending trouble; she merely stopped breathing. The Quick test on admission was 65 per cent of normal, and before operation 93 per cent.

CASE 7. A white woman, 40 years of age, had a toxic nodular goiter. Several teeth were extracted shortly after admission. A week later more teeth were extracted and the same day a gastrointestinal study was begun. Iodine therapy was instituted 41 days after admission and 13 days before death. The patient fell out of bed the day before death, and died in crisis within 24 hours. The Quick test shortly after admission was 46.5 per cent of normal.

CASE 8. A negro man, 37 years of age, had a toxic diffuse goiter with cardiac insufficiency. Thoracentesis was necessary during his preoperative preparation. He withstood lobectomy successfully, but while he was being prepared for the second stage operation was dismissed from the hospital in error, when the wards were being emptied of all but urgent cases prior to the demolition of the old hospital. When he was brought back five days later he was again in failure and was not a good risk when the second lobectomy was done. He died of heart failure 36 hours later. The Quick test on admission was 40.6 per cent of normal but improved progressively during preparation, and rose promptly after the drop which followed the first lobectomy.

CASE 9. A negro woman, 24 years of age, with a toxic diffuse goiter, did not respond to prolonged preparation and was seriously disturbed by the con-

fusion of the hospital construction and the overcrowding of the ward. She died in crisis 30 hours after lobectomy. The Quick test showed 35.5 per cent of normal function on admission and had fallen to 24.8 per cent before operation.

CASE 10. A white woman, 32 years of age, with a toxic diffuse goiter, had taken Lugol's solution for a year before admission. She was extremely restless and nervous, and was on the verge of crisis on several occasions. She developed a furunculosis and died in crisis four weeks after admission. The Quick test shortly after admission showed 32.8 per cent of normal function. Necropsy revealed toxic hepatitis with granular changes.

TABLE 6
AVERAGE PERCENTAGES OF NORMAL HEPATIC FUNCTION IN THYROID DISEASE

TYPE	PREOPERATIVE		POSTOPERATIVE (By days)			
	1	2*	1	2	3	7
Diffuse	83.2		53.8	70.2	80.0	81.5
Toxic diffuse	57.4	75.3	60.0	64.0	55.6	77.1
Nodular	77.7	94.3	70.9	71.6	74.2	72.0
Toxic nodular	55.6	73.2	66.5	71.0	66.4	73.0
Ethylene control	100.0		79.0	91.0		88.5

*After preparation.

Preoperative and postoperative values. The series includes badly prepared, routinely prepared, and intensively prepared patients. The drop in values on the third postoperative day in toxic diffuse and toxic nodular cases is to be explained by the withdrawal of intensive postoperative therapy.

TABLE 7
AVERAGE VALUES FOR QUICK HIPPURIC ACID TEST IN THYROID DISEASE BY RACIAL DISTRIBUTION

TYPE	WHITE	NEGRO
Diffuse	91.0	77.5
Toxic diffuse	55.6	59.0
Nodular	81.0	78.1
Toxic nodular	64.7	54.6

CASE 11. A negro woman, 48 years of age, with a toxic nodular goiter, showed intense toxicity and was much disturbed by the noise of the hospital construction and the overcrowding of the ward. She did not respond to any sort of preparation and died in violent crisis. Exophthalmos developed during the period of observation, and several days before death it was observed that her liver was markedly enlarged. The Quick test on admission showed 29.7 per cent of normal and the last test made, one month before death, showed 19.3 per cent.

Our collected average values in two series of cases (table 5) leave no doubt of the hepatic damage which the toxic state induces. It will be noted also that except in non-toxic diffuse goiter all the

values in the second series are lower than in the first. Part of the explanation may lie in the inclusion in the second series of three exceedingly toxic patients (cases 9, 10 and 11) who had lower values than any patients whom we have studied. Since only one test was run on one of these patients (case 10) the possibility of error cannot be entirely excluded. In the other two cases repeated tests were run, all of which showed the same low levels, and the values can be accepted absolutely.

I am inclined to believe that the lower values in the second series are due to the fact that in many instances the intravenous Quick³³ test was used, whereas all the cases in the first series were studied by the oral Quick test. For many reasons the intravenous test seems to be more delicate than the oral, and it is quite possible that the lower values in the second series reflect its more frequent use. The differences are not great, but are still sufficiently marked to be significant.

Hepatic damage in toxic thyroid patients cannot safely be ignored. Our studies³⁴ reveal a marked drop in liver function after all surgery, and the Lahey Clinic studies parallel the decreases we have noted after thyroid surgery. When patients are properly prepared, respond to preparation, and are adequately treated after operation, they are bolstered against this fall (table 6), at least until the immediate trauma of surgery is over. When they have low initial values, are improperly prepared or do not respond to preparation, and do not receive adequate postoperative care, their situation becomes dangerous and may readily prove fatal. Even in non-toxic cases that danger may arise, as a single case history will prove:

A negro woman, aged 31, with a non-toxic nodular goiter, had only mechanical symptoms. She had had the goiter for 20 years. Her Wassermann reaction was positive, and her liver enlarged. The Quick test on admission showed 37 per cent of normal liver function. Under intensive treatment with glucose and decholin, both given orally, the value rose to 87 per cent of normal. After operation, through a misunderstanding of orders, she had only routine treatment. On the second postoperative day the test had fallen to 32 per cent of normal, and on the third day to 29 per cent of normal. It had risen to only 31 per cent when she left the hospital. What would have happened if she had had no preparation at all—non-toxic patients usually have none—is an interesting speculation. It is equally interesting to observe that persistence of life with such markedly impaired liver function adds further support to Mann's experimental observations that the liver can carry on its functions when only 17 per cent of its substance remains *in situ*.

In a previous communication³⁰ I have called attention to the marked discrepancies in initial function between negro and white patients (table 7). Only in toxic diffuse disease is the average negro value for the Quick test higher than for the white. The duration of

latent or actual toxicity over a long period of time, upon which I have already commented, perhaps furnishes the explanation of this finding. Whatever the reason, the lower values for hepatic function may very possibly help to explain the higher negro mortality in toxic thyroid disease.

REDUCING THE MORTALITY OF THYROID DISEASE

The solution of the problem of a high thyroid mortality would seem to be here, as elsewhere, the reduction of the duration of the disease, with the idea of terminating the toxicity before it has wrought irreversible visceral damage. Surgery offers the most permanent, as well as the safest and promptest, means of accomplishing this end. That is, as Lahey⁴ points out, the well considered opinion of the men who are handling the largest numbers of thyroid patients today. It is certainly my own opinion.

Surgery, naturally, will not cure all patients. Some are doomed when they are first seen and will die more rapidly with operation than without it. Yet in some cases, at least, as J. M. T. Finney says, it is quite possible that we shall have done the victim a favor if, in an attempt to relieve his suffering, we have given him a quick and easy exitus to the other land.

If this small group of hopeless cases be eliminated, there is no doubt that the mortality of thyroid disease can be vastly improved whenever the medical and surgical staffs of a hospital sit down together in conference and take stock of themselves and their performance. That has recently been proved at Cook County Hospital.³⁸ With earlier recognition of the disease, with careful preoperative preparation, with accurate estimations of toxicity, with prompt surgery, graded when necessary, with adequate preoperative and postoperative care, there is no doubt that the death rate in any community, even in a general hospital, should show an equally gratifying decrease.

SUMMARY

1. The death rate of thyroid disease in New Orleans, as in all non-endemic areas, is unreasonably high. A comparison of the local and national death rates makes this very clear.
2. A comparison of the statistics for New Orleans as a whole with those of Charity Hospital of Louisiana in that city shows that the hospital statistics are not unrepresentative.
3. An analysis has been made of 817 consecutive surgical cases of thyroid disease and of 103 consecutive deaths from Charity Hospital.

4. The negro death rate is high and the negro male death rate inordinately high.

5. The number of non-surgical deaths seems disproportionately high, particularly in recent years.

6. Crisis, which was responsible for the largest number of deaths, apparently can develop at any time in any patient.

7. An inaccurate estimate of toxicity in the individual patients is one of the chief reasons for both surgical and non-surgical deaths.

8. Liver damage is an important but generally overlooked factor in the thyroid mortality. The Quick hippuric acid liver function test is a satisfactory method of estimating the degree of hepatic damage which has occurred.

9. Closer cooperation between the physician and the surgeon would seem the most practical method of improving the thyroid mortality in a community in which no single physician sees enough cases of the disease to become really familiar with its manifestations and dangers.

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REFERENCES

1. Maes, U.; Boyce, F. F., and McFetridge, E. M.: Clinical Problems of Thyroid Disease in a Non-endemic Area, *Am. J. Surg.* 24: 232, 1934.
2. Maes, U.; Boyce, F. F., and McFetridge, E. M.: Hyperthyroidism in the Negro, *West. J. Surg.* 42: 456, 1934.
3. Maes, U.; Boyce, F. F., and McFetridge, E. M.: Further Observations on Thyroid Disease in a Non-endemic Area: An analysis of 662 surgical cases and 16 Non-surgical deaths, *Ann. Surg.* 105: 700, 1937.
4. Lahey, F. H.: End-results in Thyrocardiacs, *Ann. Surg.* 90: 750, 1929.
5. Dinsmore, R. S.: Factors Influencing Morbidity in Thyroid Surgery. *J. A. M. A.* 109: 179, 1937.
6. Batchelor, J. M.: Personal communication.
7. Ranson, H. K., and Bayley, R. H.: Thyroid Crisis, *West. J. Surg.* 42: 464, 1934.
8. Plummer, W. A., and Mayo, C. H.: Surgical Operations and Associated Infections as Possible Etiological Factors in the Development of Exophthalmic Goiter and of Hyperthyroidism from Adenomatous Goiter, *Surg., Gynec. & Obst.* 53: 721, 1931.
9. Forbes, R. D.: Hyperthyroidism after Abdominal Operations, *S. Clin. N. America* 14: 1339, 1934.
10. Lockwood, A. L.: Unexpected Hyperthyroidism Postoperative, *West. J. Surg.* 45: 499, 1937.
11. Bayley, R. H.: Thyroid Crisis, *Surg., Gynec. & Obst.* 59: 41, 1934.
12. Wilensky, A. O.: Occurrence, Distribution and Pathogenesis of So-called Liver Death and/or the Hepatorenal Syndrome, *Arch. Surg.* 38: 625, 1939.
13. Lahey, F. H.: Reduction of Mortality in Hyperthyroidism, *New England J. Med.* 213: 475, 1935.
14. Hertzler, A. E.: Pathogenesis of Goiter Considered as One Continuous Disease Process, *Arch. Surg.* 16: 61, 1928.
15. Bartlett, W., Jr.: Duration of Voluntary Apnea in Thyrotoxicosis: An Index of Stability and a Criterion of Operative Risk, *Surg., Gynec. & Obst.* 63: 576, 1936.

16. Crile, G., et al.: *Diagnosis and Treatment of Diseases of the Thyroid Gland*. Philadelphia: W. B. Saunders Company, 1932.
17. Means, J. H.: *The Thyroid and its Diseases*. Philadelphia: J. B. Lippincott Company, 1937.
18. Lerman, J.: Iodine Response and Some Other Factors in Relation to Mortality in Thyrotoxicosis, *West. J. Surg.* 45: 439, 1937.
19. Eaton, A. G.: The Basal Metabolic Rates of Normal Individuals in New Orleans, *J. Lab. & Clin. Med.* 24: 1255 (Sept.) 1939.
20. Lahey, F. H.: Activated and Apathetic Hyperthyroidism; Their Importance in Cases of Heart Failure, *South. Surgeon* 1: 36, 1932.
21. Gordon, S., and Graham, R. R.: Clinical Hyperthyroidism Associated with Normal Basal Metabolic Rate, *Canad. M. A. J.* 32: 162, 1935.
22. Crile, G., and Crile, G., Jr.: Individualization of the Patient in the Treatment of Hyperthyroidism, *Cleveland Clin. Quart.* 2: 23, 1935.
23. Pemberton, J. deJ.: Goiter: Management of Poor Surgical Risk, *Arch. Surg.* 20: 591, 1930.
24. Beaver, D. C., and Pemberton, J. deJ.: Pathologic Anatomy of Liver in Exophthalmic Goiter, *Ann. Int. Med.* 7: 687, 1933.
25. Cameron, G. R., and Karunaratne, A. E.: Liver changes in Exophthalmic Goiter, *J. Path. & Bacteriol.* 41: 267, 1935.
26. Weller, C. V.: Hepatic Pathology in Exophthalmic Goiter, *Ann. Int. Med.* 7: 543, 1933.
27. Lahey, F. H.: Critical Thyroid States, Their Diagnosis and Treatment, *S. Clin. N. America.* 16: 1521, 1936.
28. Youmans, J. B., and Warfield, L. M.: Liver Injury in Thyrotoxicosis as Evidenced by Decreased Functional Efficiency. *Arch. Int. Med.* 37: 1, 1926.
29. Quick, A. J.: Clinical Value of the Test for Hippuric Acid in Cases of Diseases of the Liver, *Arch. Int. Med.* 57: 544, 1936.
30. Boyce, F. F., and McFetridge, E. M.: Studies of Hepatic Function by the Quick Hippuric Acid Test. II. Thyroid Disease. *Arch. Surg.* 37: 427, 1938.
31. Cattell, R. B.: Lecture before students of Louisiana State University School of Medicine, March 29, 1939.
32. Bartels, C., and Perkin, H. J.: Liver Function in Hyperthyroidism as Determined by the Hippuric Acid Test, *New England J. Med.* 216: 1051, 1937.
33. Quick, A. J.; Ottenstein, H. N., and Weltchek, H.: Synthesis of Hippuric Acid in Man Following Intravenous Injection of Sodium Benzoate, *Proc. Soc. Exp. Biol. & Med.* 38: 77, 1938.
34. Boyce, F. F., and McFetridge, E. M.: Studies in Liver Function by the Quick Hippuric Acid Test. III. Various Surgical States, *Arch. Surg.* 37: 443, 1938.
35. Thompson, W. O.; Taylor, S. G., III, and Meyer, K. A.: The Relation Between the Preoperative Condition of the Patient and Operative Mortality in Exophthalmic Goiter, *Illinois M. J.* 67: 53, 1935.

PRIMARY OVARIAN PREGNANCY

Review of the Literature and Case Report

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OVARIAN pregnancy is rare indeed. It has been stated that Maurice laid claim to the first reported case in 1682. Spiegelberg¹ formulated four criteria in an effort to clarify the dubious claims prior to 1878. Van Tussenbroek² in 1899, Thompson³ in 1902, and Norris⁴ in 1909 were some of the early authors who have reported cases. Some believe that there have been eighty-five proven cases to date.

We have reviewed the reports of those cases which answer the requirements of the accepted criteria and have found a total of fifty-two to date, including the one which we are reporting, and every one of these cases complies with the classification for primary ovarian pregnancy as set forth by Sutton⁵. The classification of the primary and secondary type is as follows: The primary type is one in which the fertilized ovum undergoes a certain stage of its development entirely within the ovary; the secondary is one in which the ovum, following its fertilization, undergoes a certain stage of its development in some nearby structure or cavity, usually the fallopian tube, and then becomes implanted upon the ovary. Many of the reported cases of primary ovarian pregnancy were not substantiated by serial sections of the salpinx on the involved side and some of the cases might have been fallopian tube gestation with a secondary implantation upon the ovary. No doubt there have been many primary ovarian pregnancies which are not reported.

We submit the following case as a proved primary ovarian pregnancy:

Mrs. T. H., a 23 year old woman pregnant for the second time, was admitted to the John Gaston Hospital from the Prenatal Clinic on Sept. 28, 1938, diagnosed as a possible threatened abortion in the first trimester. Upon admission the physical findings were as follows: Profuse perspiration over the entire body, cold and clammy, respirations 22 but labored, pulse 60, temperature 98.6, and some bleeding from the vagina. The patient complained of nausea and severe pain in the lower abdomen. The admission laboratory report revealed 26,700 white blood cells with 71 per cent polymorphonuclears, 3,570,000 red blood cells, 9.3 Gm. of hemoglobin, and the urine essentially negative.

From the University of Tennessee, College of Medicine.

The past history was as follows: The patient had had the usual childhood diseases. She had had typhoid fever in 1931, malaria in 1929, but no injuries or operations. Menstruation established at 14 with a normal flow had been regular, lasting three days, until the gestation and delivery in 1933. The patient had been regular since then but with an unusually small amount of flow associated with severe abdominal cramps beginning one week before the onset of menstruation. No contraceptive methods had been used. Her last monthly period was on July 25, 1938. She had gained weight excessively during the previous year and weighed 226 pounds at the time of admission.

The senior essayist saw the patient a few minutes after admission and made the following note:

"On Sept. 14, 1938 she began having abdominal cramps with vaginal spotting. These recurred almost every other day until the present date, and they were more severe on the left side. With an almost classic history of ectopic pregnancy, I believe this patient's left salpinx is involved because her condition suggests the left side. The abdomen is slightly rigid over the lower quadrants, and she complains of the pain travelling to the xiphoid process. The upper quadrants are becoming more rigid as the minutes pass. The patient is in no condition for a pelvic examination, and I suggest this should be done just before the operation.

"Impression: Ruptured ectopic pregnancy on left.

"Treatment: Supportive and emergency laparotomy."

Morphine sulphate, gr. $\frac{1}{4}$; caffein sodium benzoate, gr. viiss; atropine sulphate, gr. 1/150, by hypodermic, and a fusion of 1000 c.c. of 5 per cent glucose were administered before the operation. The patient was catheterized.

"A sterile vaginal examination revealed a small uterus which was almost normal in size, anteverted, freely movable, one degree bilateral laceration of the cervix, and no palpable masses of the adnexa. An ovary, approximately 3.5 cm. in diameter, was palpated on the right but none was palpable on the left. Neither salpinx was enlarged. The inferior vaginal vault was under some pressure due to a soft mass in the culdesac. Second degree cystocele and rectocele were present. Chadwick's and Ladin's signs were negative. Tincture of metaphen was instilled in the vagina.

"Impression: Ruptured ectopic pregnancy lying in the culdesac."

Nitrous oxide and a small amount of ether were used as the anesthetic. A transfusion was started by the indirect method, using 500 c.c. from the "blood bank." A midline incision revealed free blood in the peritoneal cavity. The superficial clots were removed. Both tubes were normal and the right ovary was slightly cystic. The left ovary was not found in its normal position. Blood spurted upon raising the uterus ventrally and the examining hand removed a soft mass of bloody tissues from the culdesac. This mass consisted of a placenta and a fetus. The left tube was intact but the left ovary presented a bleeding crater, approximately 2 cm. in diameter, to which placental tissue adhered. The uterus was normal in size, color, and consistency. Left salpingo-oophorectomy was performed. The severed edges were covered with peritoneal reflections and the abdominal wall closed. Smears and cultures were taken from the culdesac. The immediate postoperative condition was fair with a pulse rate of 100 and of good volume, blood pressure 90/60, and a respiratory rate of 30.

The postoperative treatment was the usual rest, supportive drugs, infusion of Hartmann's solution in 1000 c.c. of 5 per cent glucose b. i. d. for two days, and the usual postoperative diets.

Nausea the first day, two days of morbidity, an easily controlled slight distention, and serum drainage from the wound were the complications. The blood pressure, pulse and respirations gradually improved in character as the days passed and the patient's only complaint was an occasional headache. The patient was discharged on the thirteenth postoperative day. The aforementioned anaerobic culture was reported negative and the aerobic culture was contaminated.

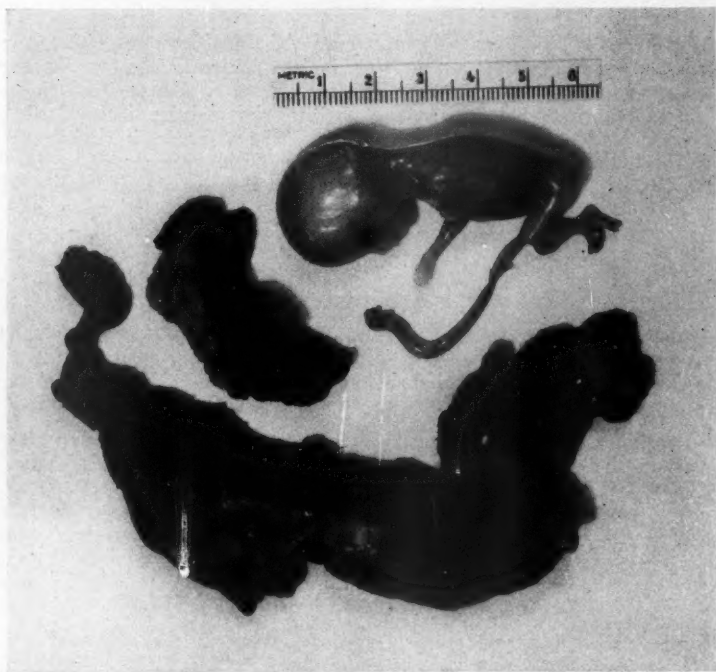


Fig. 1. Gross operative specimens. The age of the fetus is estimated at 13 to 14 weeks (Streeter's rule). There has been some shrinkage due to the preserving fluids.

On Apr. 1, 1939, the pelvic examination was essentially negative. The abdominal scar was strong and the patient had no complaints. She was discharged in good condition.

PATHOLOGIC REPORT BY DR. W. W. BRANDES

Macroscopic: Specimen consisted of an ovary, fallopian tube and broad ligament, and a fetus of 78 mm. (crown-heel-length). The fetus showed no evidence of malformation or other pathologic changes (fig. 1). The fetal membranes were torn but adherent to the ovary at the site of laceration.

tion. A soft, grayish-red, friable mass, measuring 15 by 35 mm., which had been separated from the other structure, was of typical placental tissue.

The salpinx measured 5 cm. in length. Its surface was hyperemic. At the fimbriated end were masses of clotted blood and fragments of adherent grayish tissue. Longitudinal section of the tube revealed an edematous, hyperemic mucosal lining. The lumen was patent throughout.

The ovary measured 2.5 by 15 cm. in its greatest dimensions. There was a laceration 2.2 cm. in its greatest diameter, to which point fetal membranes were adherent. The cavity, 12 mm. in depth, exhibited a ragged lining riddled with a blood clot. On section, a corpus luteum measuring 2 by 7 mm. was seen.



Fig. 2. Portion of ovary containing a part of the convoluted layer of lutean cells making up the corpus luteum. Magnified 200 times.

Microscopic: Sections taken through the edge of the lacerated area in the ovary revealed edematous ovarian tissue. Hemorrhage and a fibrin clot were present. In one portion was a convoluted layer of lutean cells (fig. 2). The ovarian tissue in the adjacent areas was intimately intermixed with the chorionic villi of the placental tissue (fig. 3). These showed the Langhans cell layers and syncytial masses very distinctly. Several small follicles were present in the adjacent ovarian tissue. Some had blood in the cavities (fig. 4).

Section from the fallopian tube, 1.5 cm. from the fimbriated end, exhibited edema and hyperemia. The mucosal papillae were somewhat thickened due to edema and an increase in stroma. Mild lymphocytic cell infiltration was seen. Some of the blood vessels had an increased number of polymorphonuclears in the lumina. The mucosa was intact everywhere, and no placental tissue was present (fig. 5).

In a section taken from the fimbria of the tube adherent blood clot but no placental tissue was seen.

Section taken from the broad ligament, which was not thickened in the gross, revealed some edema and hemorrhage into the tissues. On the wall

of an irregular space (apparently vein) there was a small fragment of a chorionic villus.

Study of these sections seemed to rule out placentation of the tube or broad ligament. Primary ovarian implantation was a justified conclusion from the gross and microscopic study.

DIAGNOSIS: 1. Ovarian pregnancy, primary. 2. Salpingitis, chronic.

COMMENT

There have been some to assert that the proof of primary ovarian pregnancy is a normal pelvis with a ruptured ovary containing a corpus luteum and chorionic villi in the clot. It seems to



Fig. 3. Section from ovary showing placental tissue with typical chorionic villi. Magnified 200 times.

us that this cannot be true, because the products of conception may have been formed in the salpinx, then expelled into the abdominal cavity to become implanted upon an ovary. It is true that the developing embryo would not remain for long in the abdominal cavity without some blood supply, but very early it could imbibe nourishment from the serous secretions in the peritoneal cavity until it became implanted. Such cases do not completely comply with the accepted criteria for primary ovarian pregnancy. The epithelial lining of the cavity of the graafian follicle is the only structure in the ovary adapted to the nidation of the fertilized ovum. It is possible that the ovum might not be expelled from the follicle when the theca interna and externa rupture, at which time the liquor and ovum are usually expressed in order to complete the cycle typical of ovulation.

It is reasonable to assume that all primary ovarian pregnancies follow pathologic changes in the ovary when ovulation is prevented as the result of improper stimulation by the hypophyseal hormone which causes the thecae to rupture. Numerous graafian follicle cysts of various sizes were found intact in the ovarian stroma of our specimen; therefore, there must have been an abnormal condition preventing ovulation. The following are possible explanations of the phenomenon which occurs: (1) Some have suggested that there is a gradual oozing of the liquor from the follicle and that the spermatozoon might enter during this slow process; (2) the theca may become so thickened at the time of rupture that these retard or retain the ovum within the follicle; (3) again, the ovum

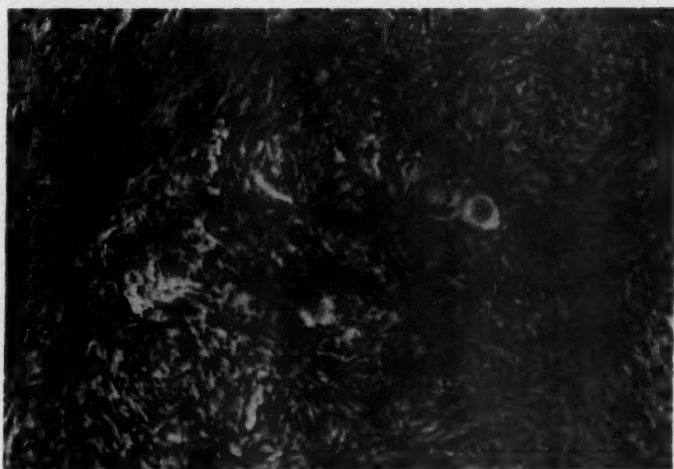


Fig. 4. Field adjacent to Figure 3, revealing characteristic ovarian stroma in which two small primordial follicles containing ova are seen. Magnified 200 times.

may be attached more firmly than normal to the discus proligerus, so that rupture occurs without the extrusion of the ovum. The stratum granulosum is never expelled except under pathologic circumstances, so the ovum remains attached and may be fertilized in the ovary.

We would like to add to the accepted criteria by postulating further that the serial sections of the salpinx on the affected side must prove that no rupture has occurred. It would be difficult for anyone to lay claim to a primary ovarian pregnancy without these sections because, whenever the developing embryo is implanted upon the ovary, it is at the site of a reasonable blood supply which would most likely be furnished by a ruptured graafian follicle.

Because the trophoplasts burrow into the clot to gain nourishment for the developing embryo, this seems to be a logical answer to the question, why the villi are found in the blood clots of those cases which (in our belief) are probably of the "secondary" type.

No epithelial lining could be located in our specimen, but it is logical to assume that these cells degenerated as the result of pressure from so large a fetus, just as is true in some specimens of ovarian cysts. Some authors have reported that no corpus luteum was found upon sectioning the ovary, but we do not believe that this finding is absolutely necessary, because it would be difficult to examine every portion of the ovarian tissue and a very small corpus luteum may be overlooked for this reason.



Fig. 5. Section of fallopian tube near the fimbriated end revealing edema and lymphocytic infiltration of the wall and absence of placental elements. Magnified 75 times.

Many of the reported cases have mentioned periods of sterility previous to the ovarian pregnancy. Sutton⁵ and Bass⁶ reported interesting accounts of patients never having been pregnant prior to the ovarian pregnancy although married for a period of years. Wollner⁷ reported that the pregnancy in his case was preceded by 16 years of barrenness. Our patient experienced $5\frac{1}{2}$ years of sterility although married. However, there were few who reported periods of amenorrhea prior to conception. Whatever be the processes that take place, the ovum remains unfertilized in the follicle if no spermatozoon enters and sterility results, as proved by the histories of those cases reported. Again, some graafian follicles

may not develop beyond the stage noted by Simkins⁸ in the five months fetus. Maturity of these may be retarded for many years, may become large and vesicular and then degenerate, as Pankratz⁹ observed.

CONCLUSIONS

1. The retention of the ovum in the follicle results from some pathologic change such as inflammation, thickening of the theca, a dormant follicle, or a stronger than normal attachment by the discus proligerus to the ovum.

2. Cases of true primary ovarian pregnancy are preceded by periods of sterility.

3. Serial sections of the salpinx examined microscopically are required to distinguish between primary and secondary ovarian pregnancies, in addition to complying with all the accepted criteria.

4. Follicle cysts are present in the stroma of the ovary in the specimen of the primary type.

5. Our specimen proves this case to be a primary ovarian pregnancy because neither salpinx was attached to the ovary and the requirements of the foregoing criteria have been fulfilled.

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REFERENCES

1. Spiegelberg, O.: Zur Kasuistik der Ovarialschwangerschaft, *Arch. f. Gynaek.* 13: 73, 1878.
2. Van Tussenbroek, C.: Un cas de grossesse ovarienne, *Ann. de gynec. et d'obst.* 52: 537, 1899.
3. Thompson, J. F.: Ovarian Pregnancy with Report of a Case, *Am. Gynec.* 1: 1, 1902.
4. Norris, C. C.: Primary Ovarian Pregnancy and the Report of a Case Combined with Intra-Uterine Pregnancy, *Surg., Gynec. & Obst.* 9: 124, 1909.
5. Sutton, L. A.: Ovarian Pregnancy; Report of Case, *Am. J. Obst. & Gyn.* 7: 1, 1924.
6. Bass, F.: Ovarian Pregnancy; Case, *Centralbl. f. Gynaek.* 52: 1640, 1928.
7. Wollner, A.: Ovarian Pregnancy; Case with Comments on its Etiology, *Am. J. Obst. & Gynec.* 23: 262 (Feb.) 1932.
8. Simkins, C. S.: *Textbook of Human Embryology*, 1931, 8-14.
9. Pankratz, D. S.: Some Observations on the Graafian Follicles in an Adult Human Ovary, *Anat. Rec.* 71: 211 (Jan. 25) 1938.

BONE TUMORS

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THE confines of this article necessarily allow no great detail on such a large subject, but I feel that any effort to present a prospectus that might be of some value to the physician who has neither the time nor the advantages for intensive study in this field will not be wasted.

After first noting that bone tumors either are primary in bones or secondarily involve them, the simplest concept, it seems, is to consider the primary tumors in two groups, viz., those which have a relationship to various stages or processes of osteogenesis and those which do not. In the former group are found the benign osteochondromas or exostoses, osteomas, chondromas or chondromyxomas, bone cysts or osteitis fibrosa, and giant cell tumors. Osteogenic sarcomas comprise the malignant ones. In the latter group (those which have no relationship to osteogenesis) are found Ewing's sarcoma and multiple myeloma. Secondary involvement of bone is by metastasis from a primary tumor outside the bone, the chief offender being carcinoma, or by contiguity from a tumor adjacent to bone, the chief offenders being carcinoma, fascial and neurogenic sarcomas. A host of developmental, metabolic, endocrine, lymphatic and blood disturbances may cause bone changes, but to avoid confusion will receive short shrift here except when noted for differential diagnosis. In this field, as in all pathology, neoplasms must be distinguished from the ubiquitous pyogenic, tuberculous, and syphilitic infections. A workable rule to follow is to consider lesions which involve both sides of a joint as benign or infectious rather than attributable to a malignant tumor. Arthritis, tuberculosis, trophic joint disturbances, as in Charcot's joint or syringomyelia, are examples, while it is practically unknown for an osteogenic sarcoma to bridge a joint and involve the other bone.

We are more fortunate than our predecessors in having the x-ray as an aid in diagnosis and therapy. Previous to its introduction into medicine the study of bone lesions was limited to clinical, operative, histologic and autopsy findings. Of course even the roentgenograms may be confusing at times, or not diagnostic in all cases, but, by and large, much valuable information can be obtained therefrom. The important point is that the roentgenogram is essentially an aid, constituting only a part of the information relative to a given case, and

This paper was prepared while the author was a trainee of the National Cancer Institute, Johns Hopkins Hospital, Baltimore.

dogmatic interpretation is frequently hazardous. Especially is this true now that radiograms are being used more generally and the earlier stages of bone affections are being seen. Recently, in this Laboratory, a clinic was held, the purpose of which was to bring home to radiologists the fact that so-called characteristic radiograms sometimes turn out to represent something entirely different. Our knowledge of bone tumors is still relatively meager, and new developments in this field, as in all branches of medicine, gradually change opinions and diagnoses. For example, it was only in 1921 that Ewing¹ described his solitary diffuse endothelioma of bone. Theretofore the diagnoses were usually round cell sarcomas or myelomas. Now some investigators believe this tumor to be a sarcoma of the bone lymphatics. Likewise we are beginning to recognize more cases of synoviomas or synovial sarcomas (arising from joint and bursal² linings) as entities and separating them from osteogenic tumors and metastatic carcinomas.

Given a patient with a bone lesion the uppermost question in the mind of the physician is "Is it a tumor, and if so, is it malignant?", for hereon may hinge the life of the patient and most certainly the advice and treatment to be recommended. At the outset it should be remembered that the age incidence for malignant bone tumors (sarcomas) is different from that for carcinoma, i.e., sarcomas afflict those in the earlier decades and carcinomas those in the later ones, due allowance always being made for individual exceptions. As tumors of bone are closely related to bone developmental processes it is apparent that they will be more frequent in those years when bone is "a-building." In the adult and ebbing years there is not so much going on in bone and consequently less chance for neoplastic dissociation. Cancer, on the other hand, is not related to developing processes, at least as regards its immediate causal factor, and whatever these causal factors may be (released control, nutritive changes, chronic irritation, chronic lymphangitis, lost organization, degenerative overgrowth, or any of the other myriad hypotheses), it occurs nearer the distal end of life's span.

Hertzler³ proposes a general rule in deciding on benignity or malignity. It is that "Bone malignancies are characterized by the fact that they both produce and destroy bone. In proportion in which a bone lesion is either proliferative alone or destructive alone it is likely not to be malignant." Bearing this out we find that the benign exostoses and osteomas are bone proliferating; the benign chondromas, although cartilage proliferating, are bone destructive; benign giant cell tumors are essentially bone destructive while the sarcomas are both bone forming and bone destructive. Exceptions

to be noted are the osteolytic form of osteogenic sarcoma which is destructive alone, although malignant, and multiple myeloma which is also bone destructive alone although a fatal disease. A characteristic of the malignant Ewing's sarcoma is widening and increased density of a bone shaft, but this increased density is caused by nature's defense of reactive new bone rather than bone production by the tumor itself which is only bone destructive. To show further benign and malignant characteristics of different bone tumors it will be necessary to review these tumors individually.

The benign osteochondromas (exostoses) are so called because they consist of both cartilage and bone. They occur near the ends of the long bones in the second and third decades and bear a relation to the sites of tendon attachments. There may be one or many. A form of multiple exostoses is known as hereditary deforming chondrodysplasia (Ehrenfried⁴). This disease has recently been reviewed by Graney⁵. A report is made of 10 cases occurring in one family. The single growths are of little consequence and frequently the patient is unaware of their presence. Occasionally a lump is felt or some discomfort on joint motion has been experienced. A small percentage may undergo malignant change and this transformation may be recognized by more or less sudden and rapid growth accompanied by some pain. Renewed growth after the age period of bone growth has been reached and passed (25-30 years) is especially suggestive of malignant change. The x-ray may then reveal a more hazy appearance with proliferating bone spicules. The normal x-ray appearance reveals a broad or thin base in which the cancellous and compact bone are differentiated and are continuous with the cancellous and compact layers of the parent bone. These growths can be looked upon as exaggerated or enlarged bony protuberances for tendon attachments and not necessarily as neoplastic growths. Assuring the patient of their benignity is usually the only treatment needed but, of course, they can be chiselled off if desired. It is best, however, to refrain from continued attacks on recurrences in this manner for fear of instigating malignant change. There are some exostoses, as is well known, which occur on the os calcis and bear a relationship to gonorrhea. Hertzler³ himself is witness to the fact that there may be other causes for their occurrence in this location.

Osteomas are of the same gentle breed as the osteochondromas and differ from them only in their location and manner of histogenesis. They usually occur in the frontal and parietal bones of the skull and the maxillary bones of the face. In the latter sites they may grow to considerable size and have been referred to as "dog-faced" tumors. Their origin is by direct ossification in fibrous tissue

in contrast to the osteochondromas which pass through an intermediate cartilaginous stage. This manner of growth parallels the normal histogenesis in the membranous bones of the face and skull. Depending on the completeness of ossification these osteomas may be spongy or eburnated with intermediate gradations. The x-ray usually reveals a spotty increased density, variable in degree depending on the type. Sometimes there is seen a circumferential ring of increased density which corresponds to the region of subperiosteal calcification. Meningiomas of the brain coverings will occasionally stimulate a productive hyperostosis of the skull which in the roentgenogram may resemble an osteoma or even an osteogenic sarcoma on account of the radiating spicules. Nervous symptoms or manifestations may help one to arrive at a distinction. Irradiation treatment had better be omitted as no real benefit is obtained therefrom and besides, in children and young adults, deformities as a result of interference with regional normal bone growth and development may result. In fact the possibility of retarded bone growth must always be guarded against when irradiation is used in children, whatever the purpose. Newcomet⁶ particularly has repeatedly called the profession's attention to these late bone deformities—skin damage is not the only bad sequela. If necessary to do anything, paring off of the excessive bone is recommended.

Chondromas are generally considered benign, and this is true when they are found in their usual sites, the bones of the fingers and toes. Occasionally, however, they occur in the long bones and sternum and in these locations seem to possess greater malignant potentiality and ability to recur. These latter are the "myxomas" which Bloodgood⁷ popularized in this country but which, as he said, were first clearly described by Soubeyran of France in 1904. Kolodny⁸ suggests that the poorer prognosis of these "myxomas" in the long bones is due more to technical difficulties of adequate removal rather than to greater potential malignancy. In this Laboratory it is the custom to regard chondromas in the hands and feet as benign regardless of their pathologic appearance. The age incidence is from about 20 to 30 years. The roentgenogram shows a shell of bone surrounding an expanded, trabeculated, cyst-like area. Geschickter and Copeland⁹ regard these chondromas histogenetically as representing supernumerary joint cartilages. Bone cysts or osteitis fibrosa may cause a confounding picture and the punched out areas of gout may show slight similarity. Rarely does carcinoma metastasize to such distal regions but I have in mind one case of carcinoma of the cervix which metastasized to a metacarpal bone and there produced a rounded area of bone destruction which, how-

ever, showed no bone shell. Irradiation is of no value in therapy. Excision or careful curettage with possibly some form of cauterization is recommended, the chief thought being so to proceed as to prevent the possibility of a recurrence.

Osteitis fibrosa is a general term used to denote various cystic processes. These include the solitary bone cyst and variants of the bone cyst, such as the acute cyst, polycystic and multiple cystic states (von Recklinghausen's disease¹⁰). The solitary cyst is by far the most common. The age incidence is under 21 years and usually between the tenth and fifteenth years. The site of predilection is in the long bones, usually centrally located in the metaphysis. The three most common sites are the upper shaft of the femur, humerus, and tibia. Spontaneous fracture is a frequent complication. The roentgenogram reveals a central rarefaction in the region of the metaphysis, or in the older (latent) cysts, further in the shaft. The contours are regular, the bone is expanded, the cortex is intact. There may be trabeculations within the cystic area and the resultant appearance has earned for it the designation of "soap-bubble" tumor. This descriptive term, however, fits just as well or better the more uncommon bone angiomas.

What is known as the acute bone cyst is probably an intermediate stage between the typical bone cyst and the giant cell tumor. This type of cyst seems to produce symptoms earlier and its progress is more rapid than the ordinary cyst. The polycystic state may be an early stage of the solitary cyst before the various small cysts have amalgamated into one, or it may represent the beginning stage of the multiple cystic variety commonly known as von Recklinghausen's disease. This multiple cystic state is now considered to have a relationship to hyperparathyroidism which causes a greater excretion of calcium than normally. It is progressive unless the hyperparathyroidism is overcome either by irradiation or surgery of the parathyroids. Paget's disease of bone (osteitis deformans)¹¹ is also a disease which produces cystic changes as well as bone proliferation. It is a disease of later adult life. Many bones may be involved but the most striking changes are seen in the tibias and femurs, where the spongy, cystic bone results in a characteristic bending deformity, and in the skull where bone proliferation produces the so-called "nigger-wool" appearance in the roentgenogram. The disease is chronic but progressive, there is no known etiology, and no efficacious treatment. Secondary sarcoma may develop in a small percentage of Paget's cases.

Irradiation may be of value in the treatment of the acute cysts which, as we have seen, approximate the character of giant cell

tumors. For the ordinary solitary cyst, which must first be differentiated from Brodie's abscess, chondroma, and possibly metastatic carcinoma, one needs to destroy the fibro-osseous wall and preferably fill in the space with bone chips or a graft. This manner of treatment, of course, follows the general surgical rule of removing fibrous walls of sinuses or old abscess cavities and obliterating the space. Following pathologic fracture through a cyst nature may be able to abolish the space in the course of repair of the fracture.

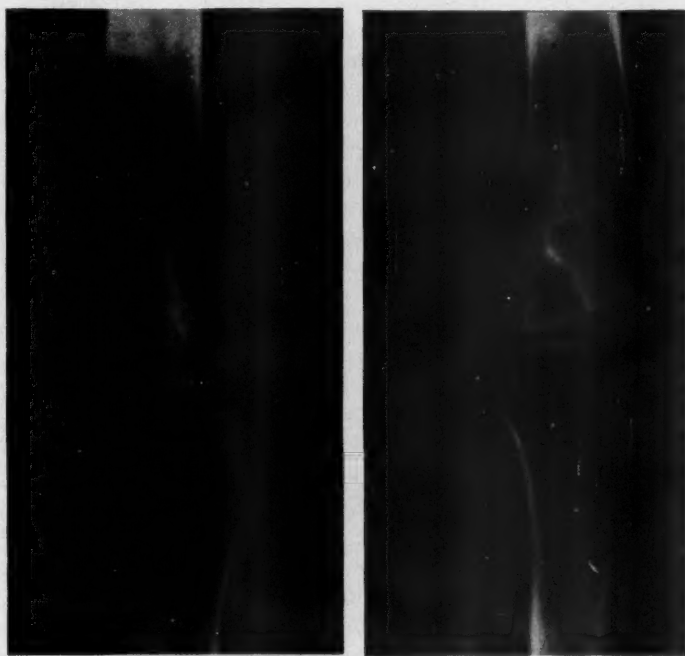


Fig. 1. Giant cell tumor. Typical location and appearance. Male, 26, pain and swelling region of left knee. In the antero-posterior view is seen a rounded area of slightly increased density situated in the center of the bone destruction. This has the appearance of a sequestrum which should not be present in a giant cell tumor. The lateral view shows that this area of increased density is situated outside the bone and that it is a sesamoid bone. This tumor was cured and the cavity filled with bone chips. A good result was obtained.

Giant cell tumors occur later than the bone cysts—an approximate average age is 28 years. Its site of election is in the epiphysis, asymmetrically located, and it usually affects the lower femur, upper tibia and lower radius. Pathologic fracture is not so frequent as in bone cysts due to the fact that the symptoms such as swelling, pain, and dysfunction are more pronounced and the patient becomes more careful of his physical activity. The x-ray shows in a typical

case (fig. 1) a rarefaction of bone situated to one side in the region of an epiphysis. There is expansion of bone and the cortex becomes very thin, frequently breaking. There seems to be no periosteal reaction. There may be some slight haziness and trabeculation within the area of rarefaction. The joint cartilage usually resists the advance of the tumor into the joint.

These giant cell tumors are the ones which, through the years, have been objects of much study and diverse opinion. Bloodgood⁷, in 1912, proposed the term "giant cell tumor." Theretofore they had been called giant cell sarcomas but numerous investigators had noted that they generally pursued a benign course (Paget¹¹, Nélaton¹², Gross¹³). Gross, in 1879, wrote an excellent article on all points of interest regarding these tumors. Codman¹⁴, first registrar of the American College of Surgeons' Bone Registry, refers to this article of Gross' as being "still the most outstanding article on this subject ever written in this country." Gross recognized the benign course of these tumors but regarded them as sarcomas because occasionally one would metastasize. Bloodgood⁷ was interested in the fact that his follow-up cards to these patients were answered by the patients themselves whereas most of those to patients with other types of sarcoma were not. In 1902 he decided that the benignity of these tumors did not necessarily require amputation or excision as was the usual practice and proceeded to treat a case by curettage. Ten years later (1912) this patient was still well. Later on Bloodgood suggested and practiced the use of bone chips or grafts to promote filling in of the cavity.

The nature and portent of the giant cells in these tumors has been and still is a matter of some argument. Mallory¹⁵ in 1911 pointed out that, in addition to true tumor giant cells, there were other giant cells of a foreign body type which differed in no respect from giant cells of the same type occurring in tuberculosis. For this reason he, also, suggested that the term giant cell sarcoma be discontinued.

Nowadays the benignity of the ordinary giant cell tumor is unquestioned but the occasional case that shows the characteristics of a benign giant cell tumor, yet recurs and later metastasizes, still causes confusion. These atypical cases are referred to as variants. Various views as to the real nature of these variants have been proposed, but I shall not endeavor here to pass on their merits and shall mention only a few. Geschickter and Copeland⁹ believe that many of these variants are really chondroblastic sarcomas or osteolytic osteogenic sarcomas. Codman¹⁴ has called those in the upper end of the humerus "epiphyseal chondromatous giant cell

tumors." Stewart, Coley and Farrow¹⁶ prefer to retain the name malignant giant cell tumor as they say it carries at least a definite connotation. The Registry of Bone Sarcoma also recognizes a malignant giant cell tumor. Their statistics in March, 1939, showed 19 of these malignant giant cell tumors and 357 benign ones. Coforth¹⁷ considers the giant cell tumors as true neoplasms and potentially malignant. He says that the giant cells are not reliable indices of the neoplasm's relative malignancy but that the character of the stroma does offer a fairly reliable criterion of the innocence or relative malignancy. Stone and Ewing¹⁸ suggested that a malignant neoplasm may develop from a benign giant cell tumor as the result of various treatment insults. In a few words, the story of giant cell tumor, then, is this: whereas it used to be considered as a benign variety of sarcoma with occasionally malignant properties, it is now thought of, not as a form of sarcoma, but as a benign tumor entity with an occasional "variant" which may be malignant.

The treatment of giant cell tumors depends considerably on their location and size. If possible to preserve the function of the bone, curettage and bone-chips are indicated. As much of the remaining shell of cortical bone as possible should be preserved. Excision may be necessary for advanced cases. Irradiation may be used especially if the tumor is situated in the vertebrae or skull. By whatever method of attack, however, the endeavor should be completely to eradicate the tumor at the first instance so that the increased difficulties of dealing with recurrences are avoided.

Whether bone cysts and giant cell tumors are inflammatory, neoplastic, dysontogenetic, reactive, or what not in origin, I find the theory that they are different stages of the same fundamental process to be quite tenable. I believe I am safe in saying that Geschickter and Copeland⁹ have done most to further this viewpoint. It is considered that trauma causes a subperiosteal disturbance of blood supply in a region of bone which is still developing (metaphysis for cyst and epiphysis for giant cell tumor). Natural bone processes are stimulated to an unnatural extent in that osteoclasts, which are normally present and active at these ages for the purpose of resorbing calcified cartilage preparatory to subsequent vascularization and adult bone formation, assume unbounded activity. Bone destruction results. In the case of giant cell tumors destruction remains unbounded and progressive. In the case of bone cysts nature has been able to secure the upper hand by a process of reparation termed fibro-ostosis. The relation, thus, of osteitis fibrosa to giant cell tumors is that of defense to destruction and, if successful, the cyst or healed stage of giant cell tumor is the result.

Collapse of the cyst is prevented by the reactive wall formed of new bone and fibrous tissue. Such a process in bone can be compared to cavity formation by tuberculosis in the lung—the cavity wall here is likewise formed of fibrous tissue which may also contain giant cells and even become partially calcified. Treatment in either case must consider the problems involved in collapsing the cavities.

The type of osteogenic sarcoma with which physicians seem to be most familiar is the sclerosing or sun-ray variety. This tumor makes an effort to carry out the histogenesis of bone except that there is usually no intervening cartilaginous stage. It can be conceived of as an adult or differentiated type of osteogenic sarcoma in contrast to the osteolytic variety (formerly known as malignant cyst or bone aneurysm) which is more embryonal or anaplastic. The general rule of malignant tumors is that prognosis and curability are directly proportional to the degree of adult differentiation of the cells making up the tumor, and we find the curability of these sarcomas bearing out this rule—the differentiated sclerosing type can be cured in 25 per cent of cases by early amputation while less than 10 per cent of the osteolytic cases are living after 5 years. The age incidence is 15 to 25 years. The sites of election for the sclerosing forms are in the periosteal regions of the metaphyses of the lower femur and upper tibia; for the osteolytic variety a central location in the shaft of long bones. The x-ray of the sclerosing sarcoma reveals dense periosteal radiating bone (sun-rays) with sclerosis of the marrow cavity in later stages. The osteolytic sarcoma presents a central or subperiosteal destructive area which may later dissolve away the cortex and invade the soft tissues. In other words, the x-rays reveal the chief characteristics of these two forms of bone sarcoma, i.e., bone destruction with new bone formation in the more differentiated sclerosing variety and bone destruction without new bone formation in the more rapidly growing and more malignant osteolytic variety.

Both of these types of osteogenic sarcoma about which I have been speaking occur in young individuals and represent essentially a primary growth. Examples of both types, however, may develop in older persons secondary to some previously existing benign lesion. These examples seem to be less malignant than the primary ones and it is really by their inclusion in the statistics that the 5-year survival rate of these sarcomas is elevated. The benign affections in which secondary sclerosing sarcomas develop are fracture callus, myositis ossificans, and Paget's disease. It is the secondary form of osteolytic sarcoma which causes much confusion on account of

its apparent similarity to giant cell tumor. In these tumors the foreign body type of giant cell may be present in considerable numbers but never as many as in giant cell tumors. Also the presence of plump spindle cells, large round osteoblasts with mitotic figures, and true tumor giant cells serve to distinguish their microscopical appearance from that of giant cell tumors.

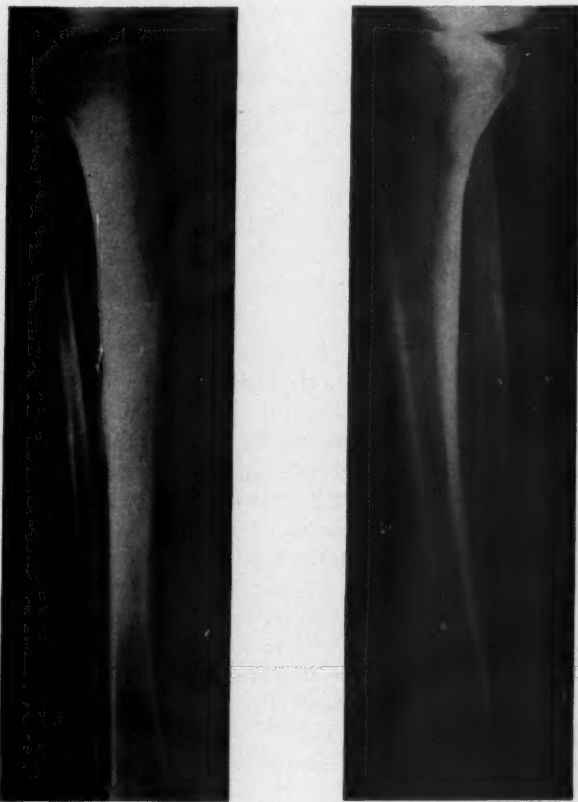


Fig. 2. Male, 35, pain over the shin. Wassermann 4 plus. Syphilis of bone. Lateral view shows periostitis on anterior surface of tibia and to a lesser degree on fibula. Antero-posterior view reveals irregular periosteal reaction on lateral side of tibia. The condition cleared up under anti-syphilitic treatment.

Conditions which may cause confusion in the roentgenogram of early sclerosing sarcoma are osteomyelitis, various kinds of periostitis such as Garré's¹⁰ non-suppurative and syphilitic periostitis, and Ewing's sarcoma. The illustration (fig. 2) of syphilitic periostitis shows a fuzzy, irregular periosteal reaction and on close in-

spection of the original film a few right angled radiations of increased density are seen. But the involvement of the fibula also and the widespread involvement of the tibia are against sarcoma. Of course, the Wassermann reaction should be known before a definite decision is made on the nature of any bone lesion. In this Laboratory there are examples of syphilitic bone involvement which had been operated on under the diagnosis of sarcoma before the Wassermann was known to be positive.

Those affections which are confusing to osteolytic sarcoma in the roentgenogram are cysts, giant cell tumors, osteomyelitis, and metastatic carcinoma. Clinically we can suspect sarcoma if, with soft part swelling, the skin is tense and shiny, the veins are prominent, and on palpation there is an elastic, semifluctuant feel. Irradiation has not yielded good results in these osteogenic sarcomas and the recommended treatment is early amputation or, in exceptionally favorable cases, excision.

Besides the sclerosing and osteolytic forms of osteogenic sarcoma there is another form which arises periosteally in about the same age group and is known as chondrosarcoma or chondromyxosarcoma. It does not produce the amount of bone seen in sclerosing sarcoma but is characterized rather by myxomatous tissue, fetal and adult cartilage. It is true, as Hertzler³ points out, that "the Registry nomenclature all but banished the prefix 'chondro' from surgical pathology," but there is a definite class of tumors in which myxomatous connective tissue and cartilage are in especial abundance. Phemister²⁰ says that these chondrosarcomas present sufficiently distinct morphologic, clinical, and roentgenologic characteristics to warrant their designation as a separate entity—and in this view I concur. They are usually primary but may arise secondarily from benign osteochondroma, chondroma, or Paget's disease and in these instances, as was also noted for the sclerosing and osteolytic sarcomas, the course is not so rapid nor so malignant as in the primary tumors. The usual sites are near joints where cartilage formation persists or where tendons are inserted. They are found most frequently near the knee joint or shoulder, involving the lower femur or upper tibia and upper humerus. The x-ray in an early case may not lead us to recognize the vast potentiality of the trouble as there is little or no early evidence of medullary or cortical involvement. The origin is not within the bone and as the myxomatous and cartilaginous tissue shows very little increased density in the soft parts, the real nature of the affection may be unnoticed or unappreciated. Sometimes the cartilage goes on to sparse bone formation and in these cases the soft parts shadow

may show small, irregular areas of increased density. Later on bone destructive areas with mottling may become evident, but the great bulk of the tumor remains outside the bone. The origin of this tumor is probably from an early type of myxomatous connective tissue related to the perichondrium. Here again irradiation does not seem to fill the bill and amputation as early as possible is the best treatment. Even then the prognosis is very bad in the primary forms and only slightly better in the secondary ones.

At the risk of causing confusion some note should be made of a tumor, the chondroblastic sarcoma of Geschickter and Copeland⁹, which forms an abortive type of cartilage. It is uncommon but rather malignant. Due to the presence of giant cells it may be confused histologically with giant cell tumor. It occurs near the age of puberty and seems to arise from the epiphyses in long bones. Malignant chondroblasts are the basic cells but they do not go on to the formation of adult cartilage or bone, preferring to stop at a stage of calcified cartilage. The x-ray shows bone destruction at the ends of long bones and sooner or later a periosteal reaction which fact makes one suspicious that it is not a benign giant cell tumor.

Of the two extra-osseous primary bone tumors (not related to osteogenesis), Ewing's sarcoma and multiple myeloma, the former is much the more common. The Bone Registry had in March, 1939, 226 cases of Ewing's tumor to 83 of myelomas. Ewing²¹, in 1922, separated this particular form of bone sarcoma from among those which had generally been diagnosed as round cell sarcoma or myeloma and classed them as endotheliomas. Of the three varieties of endotheliomas which Ewing described the one referred to as solitary diffuse endothelioma is the one which is now spoken of generally as Ewing's tumor or sarcoma of bone. Although the cell of origin is not definitely known, there seem to be some characteristics of the tumor which suggest an origin from the lymphatics of bone, especially perhaps a primitive reticulum cell⁹. The small round cells with scanty cytoplasm, their growth in sheets with sometimes broad strands of connective tissue separating the sheets, and the radiosensitivity are characteristics of the typical Ewing's sarcoma. All of Ewing's cases were under 21 years of age. It seems almost unknown in the negro and affects males twice as often as females. The tumor appears in the shafts of long bones, particularly the femur, tibia, humerus, and fibula, but also in the jaw and pelvis. Pain is a frequent symptom with some soft tissue swelling

and local heat. There are no diagnostic or abnormal blood findings except possibly slight leukocytosis. There may be some fever early in the disease but it is the rule later on after more bones have become involved, which is the usual course. The most characteristic x-ray evidence is widening of the shaft with increased density in the cortex and some destruction in the medulla which later on becomes narrowed and sclerosed. The attempt of the periosteum to defend against the progress of the tumor by laying down reactive new bone produces the so-called "onion peel" appearance. Later right angled spicules may form and as these are commonly parallel to each other and fairly fine they have been referred to as "groomed-whiskers" (Maseritz²²). The disease is fatal in 1½ to 2 years except in an occasional case, possibly one out of ten, which is cured by irradiation and then surgery. X-ray therapy may rapidly decrease the size of the tumor and this fact helps to serve as a diagnostic test. One cannot be assured, however, that the progress or the course of the disease has been checked. Amputation or resection should be performed following irradiation. The chief confounding condition is osteomyelitis and many cases of Ewing's sarcoma have been operated on under such a diagnosis. Of course, the real acute forms of osteomyelitis with chill, high fever, high leukocyte count, toxicity, etc., do not simulate the clinical characteristics of Ewing's tumor but the subacute or chronic forms might readily do so. There is never any pus in Ewing's or any other form of bone sarcoma except possibly following some operative procedure.

Multiple myeloma is a disease of advanced years. It is, therefore, in the age incidence of metastatic carcinoma and both produce somewhat similar bone involvement. The first time a case of multiple myeloma was thoroughly studied was in 1845. There were several collaborators in the reporting of this case which at that time went under the name of mollities ossium. Dalrymple²³ reported the microscopic examination of two involved lumbar vertebrae. His illustrations revealed cells which can be recognized as the plasma-like cells which we now consider to be the type cell of this tumor. Bence Jones²⁴ reported on the nature and characteristics of a new form of albumin found in the urine of the same patient. This particular albumin is now known as Bence Jones' albumin (or bodies) and is found in 65 to 70 per cent of cases of multiple myeloma. It has been found also, however, in some other diseases which show bone marrow involvement so is not pathognomonic of multiple myeloma. MacIntyre and Watson were in clinical attendance on the case and the former reported the clinical features and course of the disease²⁵. The patient was placed

on a therapy of steel and quinine and it was said that "he improved so much that he could bound over the hills as nimbly as any of his companions." We know now that untreated cases of multiple myeloma may show asymptomatic periods or periods of apparent regression. Another example of "post hoc ergo propter hoc" therapy. We must be mindful of the fact that the complete natural history of diseases should be thoroughly known else undue results might be attributed to some special therapy. Pain, at first rheumatic and vague, but later of an intense degree is an outstanding symptom. Multiple bone involvement is also characteristic, especially when the ribs, sternum, and spine are all involved. Deformities of the thorax and spine finally cause a characteristic pose or stance. Pathologic fracture is probably more frequent in this disease than in any other bone disease of adults. The x-rays reveal nicely punched out areas of bone destruction usually centrally in the medulla—occasionally a more diffuse type of destruction is seen. Irradiation may appear to check the individual lesions but the final fatal outcome of the disease remains unaltered.

Metastatic carcinoma comprises the largest group of secondary bone tumors. The primary sites are usually in the breast, prostate, kidney (hypernephroma), thyroid and lung. Carcinoma of the uterus, stomach and bowel, testicle, ovary, and bladder, as well as melanoma, metastasize to bone much more infrequently. But it is well to note right here that, although it is fine to know what *usually* happens in and to tumors, yet it must be stated emphatically that no general rule of thumb can be found to fit all cases—there are so many exceptions and variants that each case must, of necessity, be considered separately and individually. Without special ado regarding the manner or route of metastasis to bone I think we can accept both the hematogenous and lymphatic routes as participants. Primary carcinoma situated near bone, as on the lips, in the aural cavity, or on the face, may by direct growth invade adjacent bone or cartilage and then the prospects for cure are decidedly poorer.

A form of epithelial tumor found usually in the jaw but also rarely in the tibia and hypophyseal duct should be noted. This is the adamantinoma which is supposed to arise either from the so-called paradental debris or from the cells destined to form tooth enamel (enameloblasts), originally epithelial downgrowths. Why they should occur in the tibia and hypophyseal duct is as difficult for me to understand as why thyroid tissue, looking apparently normal, is also sometimes found in bones. This benign metastasizing goiter is claimed by some, however, to represent a real metastasis

from a malignant adenoma of the thyroid although pathologists might be hard put to decide on the malignant characteristics from examination of the adenoma alone. Adamantinomas show little tendency to metastasize but are very prone to recur if inadequately curetted and complete excision is then indicated.

The usual sites of bone metastases from carcinoma are in the spine, pelvis, femur especially the upper part, skull, ribs, and upper end of the humerus. The location is generally first in the medulla; later the cortex may be involved as well. Both bone destruction and bone formation may be evident in the roentgenogram but the lytic variety is the more common. Metastases from carcinoma of the prostate are prone to produce the sclerotic pictures of increased density. These metastatic deposits probably assume their sclerotic appearance from the fact that they are slow growing and nature's efforts to defend herself by reactive new bone bear more fruit.* Pain, being usually present, leads one to suspect bone metastases, especially if a cancer exists or existed somewhere in the body. Osler²⁶ liked to remind us of the cases of metastatic carcinoma in bone where the primary was overlooked. Irradiation may relieve the pain and possibly stimulate bone repair, but here again we must remember that the natural history of cancer in bones may show periods of regression. Osler used to report cases of this nature, too, such as those in which spinal metastases had produced pressure symptoms (paraplegia) but which symptoms cleared up completely due to shrinkage of the tumor without any special therapy directed thereto.

Bone metastases from neuroblastomas in children may be widespread. The syndrome was first described by Robert Hutchison²⁷ in 1907 and is referred to as the Hutchison type of metastasis. He laid stress on that most interesting skull involvement which causes a proptosis of the eye, but also noted involvement of the ribs, sternum and vertebrae. He found no deposits in the long bones but we know now that they do occur. Hutchison found it desirable to differentiate this syndrome from scurvy and chloroma. No efficacious treatment is known.

There remain to be noted those types of sarcoma which arise in structures adjacent to bone and which cause varying degrees of destruction by pressure or invasion. These are sarcomas of the soft parts; the fibrosarcomas from fascial layers, the neurogenic sarcomas from nerve sheaths, liposarcomas from adipose tissue, myosarcomas from muscle. No bone is formed by these tumors. The amount of bone destruction caused by these tumors is directly proportional to their rate of growth and malignancy and this in turn

*Possibly related to increased phosphatase production.

is evidenced by the degree of anaplasia of the type cell. In the case of fibrosarcoma we recognize the greatest degree of malignancy in the embryonal or oat-cell type and the lowest degree in the more adult fibro-spindle cell type. The neurogenic sarcomas especially are very malignant. Irradiation is a waste of time—only early amputation provides any chance for cure.

Space limitation will not permit any discussion of the bone changes that may be associated with certain diseases of bone marrow or the lymphoid system, but the fact that such changes do occur occasionally should be noted. These diseases are the leukemias and chloromas (green-tumors), Hodgkin's disease, lymphosarcoma, erythroblastic anemia, and those diseases of lipoid dyscrasias, the so-called xanthomatoses, such as Hand-Christian-Schüller's disease and Gaucher's splenomegaly. Irradiation is frequently of at least temporary value in most of these diseases.

SUMMARY

A short review of bone tumors with some remarks on their clinical course, histology, x-ray characteristics, and treatment has been attempted. Realizing that bone affections can be confounding I have, nevertheless, tried to make the point that the first and most important consideration is to decide, if possible, whether the condition is benign or malignant, for it is only on such knowledge that proper advice and treatment can be given.

I owe gratitude to Dr. Charles F. Geschickter for the privilege of reviewing the material in the Surgical Pathology Laboratory of the Johns Hopkins Hospital and for valued instruction. Geschickter and Copeland's comprehensive book "Tumors of Bone," 1936, has been of inestimable service in this study.

BIBLIOGRAPHY

1. Ewing, J.: Diffuse Endothelioma of Bone, *Proc. New York Path. Soc.* 21: 17, 1921.
2. Berger, L.: Synovial Sarcomas in Serous Bursae and Tendon Sheaths, *Am. J. Cancer* 34: 501 (Dec.) 1938.
3. Hertzler, A. E.: *Surgical Pathology of the Diseases of Bone*, Philadelphia, J. B. Lippincott Company, 1930-31, pp. 186, 132, 153.
4. Ehrenfried, A.: Multiple Cartilaginous Exostoses, Hereditary Deforming Chondrodysplasia, *J. A. M. A.* 64: 1642, 1915; 68: 502, 1917.
5. Graney, C. M.: Hereditary Deforming Chondrodysplasia, *J. A. M. A.* 112: 2026 (May 20) 1939.
6. Newcomet, W. S.: Developmental Changes following Irradiation, *Am. J. Roentgenol.* 36: 3 (Sept.) 1936.
7. Bloodgood, J. C.: Pure Myxoma of Bone, *Progrès méd.* 4: 221 (Dec.) 1906. The Conservative Treatment of Giant-Cell Sarcoma, with the Study of Bone Transplantation, *Ann. Surg.* 56: 210, 1912. Giant Cell Sarcoma of Bone, *Bull. Johns Hopkins Hosp.* 146: 134, 1903.
8. Kolodny, A.: *Bone Sarcoma; the Primary Malignant Tumors of Bone and the Giant Cell Tumor*, Chicago, 1927.

9. Geschickter, C. F., and Copeland, M. M.: Tumors of Bone, *Am. J. Cancer* 92, 187, 434, 1936.
10. von Recklinghausen, F. D.: Die fibröse oder deformierende Ostitis, die Osteomalacie und die osteoplastische Carcinose in ihren gegenseitigen Beziehungen, *Festschrift zu Virchow*, Berlin, 1891.
11. Paget, J.: On a Form of Chronic Inflammation of Bones (Osteitis Deformans), *Med. Chir. Tr.* 60: 37, 1877. *Lectures on Surgical Pathology*. London, 4th ed., p. 541, 1876.
12. Nélaton, E.: D'une nouvelle espèce de tumeurs bénignes des os, ou tumeurs a myéloplaxes, Paris, Adrien Delahaye, 1860.
13. Gross, S. W.: Sarcoma of the Long Bones, *Am. J. M. Sc.* 78: 2-57 (July) 1879.
14. Codman, E. A.: Bone Sarcoma, an Interpretation of the Nomenclature used by the Committee on the Registry of Bone Sarcoma by the A. C. S., Boston, 1925. Epiphyseal Chondromatous Giant Cell Tumor of the Upper End of the Humerus, *Surg., Gynec. & Obst.* 52: 543, 1931.
15. Mallory, F. B.: Giant Cell Sarcoma, *J. Med. Res.* 24: 463, 1911.
16. Stewart, F. W.; Coley, B. L., and Farrow, J. H.: Malignant Giant Cell Tumor of Bone, *Am. J. Path.* 14: 515-535 (Sept.) 1938.
17. Goforth, J. L.: Giant Cell Tumor of Bone, *Arch. Surg.* 13: 846 (Dec.) 1926.
18. Stone, W. S., and Ewing, J.: An Unusual Alteration in the Natural History of a Giant Cell Tumor of Bone, *Arch. Surg.* 7: 280-296, 1923.
19. Garré, C.: Einige seltene Erscheinungsformen der akuten infektiösen Osteomyelitis, *Festschrift zu Kocher*, Wiesb., pp. 43-62, 1891.
20. Phemister, D. B.: Chondrosarcoma of Bone, *Surg., Gynec. & Obst.* 50: 216 (Jan.) 1930.
21. Ewing, James: A Review and Classification of Bone Sarcomas, *Arch. Surg.* 4: 485-533, 1922.
22. Maseritz, I. H.: Personal Communication.
23. Dalrymple, J.: On the Microscopical Character of Mollities Ossium, *Quart. J. M. Sc.*, Dublin, 2: 85, 1846.
24. Jones, H. Bence: On a New Substance occurring in the Urine of a Patient with Mollities Ossium, *Phil. Tr. Roy. Soc. London*, 138: 55, 1848.
25. MacIntyre, W.: Case of Mollities and Fragilitas Ossium, accompanied with Urine strongly charged with Animal Matter, *Med. Chir. Tr. London*, 33: 1850.
26. Osler, W.: Medical Aspects of Carcinoma of the Breast, with a Note on the Spontaneous Disappearance of Secondary Growths, *Am. Med.*, (Apr.) 1901. *Medical Aspects of Cancer of the Breast*, *Brit. M. J.*, 1, (Jan. 6) 1906.
27. Hutchison, R.: On Suprarenal Sarcoma in Children with Metastases to the Skull, *Quart. J. Med.* 1: 33-38, 1907-8.

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HARVEY CUSHING—A MEMOIR

To have known Harvey Cushing is to have felt the powerful impact of his personal greatness. Merely to be in the medical profession is to have been subjected to his influence and to have lived in this time is to have profited by his life. For his memorable teaching, his superb example and his voluminous scientific writings have permeated to every center of medical learning in the world. His indefatigable search for truth, no less than his incomparable surgical skill, has profoundly influenced the teaching and teachers of medicine, and, through them, the practitioners of medicine throughout civilization.

Born in Cleveland, son, grandson and great grandson of distinguished physicians, a popular athlete while in college at Yale, Harvey Cushing graduated in medicine at Harvard in 1895, and served his internship at the Massachusetts General Hospital. His training was continued under the great Halsted at Johns Hopkins until 1900, when he went abroad for two years under Kocher and Kronecker at Berne and Sherrington at Liverpool.

During his stay in Switzerland he first became seriously interested in neurologic problems and determined to make a specialty of neurologic surgery.

In this determination by this man lies one of those rare combinations of "the man and the opportunity" upon which the great steps in the progress of mankind are based. The surgery of the brain was an undeveloped and seemingly hopeless field. Admirable but faltering attempts at progress had been made by Krause, McEwen, Horsley and a few others with no sustained success. A man less perfectly qualified than Cushing would have fared no better. In

him, however, were combined the basic surgical training at the hands of Halsted, from which soon developed a new and brilliant technic; the determination to master the growing knowledge of neurology for himself rather than to be a mere technician; the power of concentration and indefatigable industry which amazed his associates throughout his life; and finally, the will to perfection which rendered no task too small or unimportant to be done with the most meticulous care.

With his return to Baltimore in 1902, he began a series of technical improvements, clinical contributions and laboratory investigations which had placed neurosurgery on a well-established footing by the time of his appointment as Mosley Professor of Surgery in the Harvard Medical School and Surgeon-in-Chief of the Peter Bent Brigham Hospital in 1912. The twenty-one years in Boston continued increasingly fruitful and neurosurgery continued to grow and to thrive.

The Great War brought an interruption as to type of work but not as to its quality or quantity. As Senior Consultant in Neurological Surgery of the American Expeditionary Forces and Director of Base Hospital No. 5, operating for long hours, loaded with administrative duties, he still found time to keep a detailed journal¹, to make meticulous records of his cases and to publish his important papers on craniocerebral wounds which put this subject on a sound therapeutic basis for the first time. It was fitting that he was decorated by the governments of Great Britain, France and the United States for his military services.

It was appropriate that, when the time arrived for his retirement at Harvard in 1933, he should be called back to his first Alma Mater, Yale, as Sterling Professor of Neurology. There he continued to study and write with unreduced energy. In 1938 his most important monograph, *Meningiomas*, was published². On Oct. 7, 1939, just six months after the brilliant and affectionate celebration of his seventieth birthday by the Harvey Cushing Society, he died of coronary occlusion.

Adequately to discuss the achievements of Harvey Cushing is impossible here. The brilliant surgical career culminated in the publication in 1932 of the operative results in over two thousand cases of verified intracranial tumors, with an operative mortality not equalled in the world. His contributions to scientific literature, written always with clear thought, lucid style and painstaking scientific accuracy, numbered over three hundred.

As a teacher, he devoted the careful preparation to his clinics for students which made his addresses to distinguished colleagues

incomparable. His associates and pupils in neurosurgery include many, if not most of the leaders in that field in the world. But no less proud to call themselves his pupils are innumerable leaders in other fields of medical endeavor.

Despite his overflowing professional life, Cushing also stands in the forefront of the group of distinguished physicians who have been great literary figures. His magnificent *Life of Sir William Osler*, awarded the Pulitzer Prize in Letters in 1926, would seem a life's work alone to many. Numerous non-medical essays and addresses attest his ever-present literary interest and activity.

For the plaudits of the world Cushing was not ungrateful, but he allowed them neither to alter his character nor to interfere with his work. Honorary degrees from the world's seats of learning, honorary memberships in the scientific societies of nearly all civilized countries, the presidencies of many of his own country's societies were heaped upon him³, but he did not rest on his laurels. Indeed, his laurels were hard put to keep up with him.

His private life, too, was a full one. Visitors, whether distinguished guests or humble members of his house-staff, were always welcome in his home. He was fond of tennis and spent many hours training a cocker spaniel named Red Pepper to perform impudent imitations of friends or prominent people.

But his real hobby was an incorrigible medical bibliophilia. With characteristic thoroughness, he became an absorbed and scholarly student and collector of early medical publications. He was fond of joking that the dealers knew him as an easy mark. Undoubtedly, his great knowledge of early medical literature contributed greatly to the scholarly style of his writings, which are rich in apt quotations from and appropriate references to the works of pioneers in medical science.

Nowhere was Harvey Cushing's personality better demonstrated than in his correspondence. Busy as he was, no letter was too unimportant to receive his personal reply. Replete with dry humor, sometimes penetrating in their criticism, often affectionate in their tone, always beautiful in their diction, his letters will make the task of future biographers a joyful one.

A hard taskmaster, he drove himself harder than the rest. Intolerant of slovenliness in others, he was incredibly thorough himself. Austere and difficult to approach at times, he was nevertheless loved by a host of pupils and colleagues.

The loss of Harvey Cushing is irreparable but his influence will terminate only with the history of man.

—COBB PILCHER, M. D.

THE CONGRESS IN PROSPECT

NINETEEN-FORTY! A New Year and a New Decade. The Southeastern Surgical Congress celebrates another birthday and, at the same time, the tenth anniversary of its existence. The past ten years have been eventful ones. Growth and progress have been phenomenal. But the course has not always been smooth. The waves have been a bit boisterous in places, and shoals have appeared from time to time, yet the officers have brought the associational ship through the ten year voyage without mishap, and with but few obstructing barnacles still clinging to the hull. To have prospered under such adverse conditions proves beyond any doubt the need for our organization and assures its place among other worthy assemblies of the nation.

What of the future? At the beginning of this new decade chaos reigns in the professional as well as in the business world. Will conditions in the profession grow worse? That depends upon our attitude. Let us not lose hope. Out of mysterious Time the days will continue to come, each holding a candle between yesterday and tomorrow. The light will shine dimly backward, but the rays will not gleam ahead to illumine the uncharted pathway. Hedged about by darkness, the profession must cling firmly to the ideals which have been its rod and staff throughout the centuries, trusting that by so doing it may disperse the evils which threaten from many sides and may ultimately proceed unimpeded along the clear path of progress.

Members of the Southeastern Surgical Congress can do much toward stabilizing conditions in our territory by uniting forces in an effort to uphold and put into practice the ideals and aims of the Congress, which, briefly stated, are: (1) To stimulate progress in medical science in the southeastern part of the United States and neighboring territories; (2) to cooperate with associated medical schools and hospitals for higher standards of medical education; (3) to elevate the standards of surgery; (4) to establish a standard of competency and character for practitioners of surgery; (5) to provide for the selection of physicians adequately trained and properly qualified to practice surgery; and (6) to hold professional and social meetings, and to publish transactions. The Congress should endeavor to take advantage of every opportunity to fulfill these splendid purposes. Its success is certain if the members keep faith and keep striving.

To date, ten annual meetings of the Congress have been held and all have been well attended. Most of the material offered has been of the highest type, deserving the praise received. Several speakers from outside the territory have appeared on the programs and their

work has been inspiring and instructive, though not superior to many of the presentations of men from our own section. A number of surgeons have expressed themselves as favoring the type of program provided in preference to those of other, similar associations. The Congress urges Southern men to report their work at the meetings and to publish it in *THE SOUTHERN SURGEON*.

Secretary Beasley writes, "One feature of the Congress which has proved to be a most valuable part of its activity is the State Clinical Conferences." These conferences are held in small towns and rural hospitals for the purpose of taking clinical surgery to the doctors who cannot, or through lack of interest do not, go to the teaching centers for postgraduate work. These meetings provide an excellent means of carrying out some of the ideals to which the Congress has dedicated itself. Their popularity is attested by the warmth with which they have been received and by the fact that the local men have expressed an eagerness for their return. All the states will do well to organize state chapters as early as possible, for it is only through such local meetings that the influence of the Congress can be spread to untouched territory and the benefits of the organization can be widely recognized.

THE SOUTHERN SURGEON is an excellent journal. Its circulation heretofore has necessarily been limited, yet its pages have been read to the four corners of the nation. Beginning with the new year and the new decade, the journal will be published monthly and its circulation will be materially increased. The Congress is proud of its official organ and will support it to the limit during this year.

The Birmingham surgeons are preparing for a banner meeting on March 11, 12 and 13, 1940. Everything they have undertaken in the past has been done well. The Alabama members are enthusiastic about the Congress, and the success of the meeting is therefore assured. The Program Committee will furnish an outstanding group of teachers and speakers, and the material will be varied to gratify the taste of every one. The attendance should reach at least one thousand.

We have a fine association, its membership comprising the ablest surgeons in this section, all pledged to a noble and much needed service. Let us carry on through this new decade tirelessly, fearlessly, and in a spirit of cooperation and amity, that we may, at its close, look back upon a work well done, and turn our faces forward toward new fields to be conquered in the crusade for the advancement of medical and surgical science.

R. L. SANDERS, M. D.,
President.

BOOK REVIEWS

The Editors of THE SOUTHERN SURGEON will at all times welcome new books in the field of surgery and will acknowledge their receipt in these pages. The Editors do not, however, agree to review all books that have been submitted without solicitation.

PERIPHERAL VASCULAR DISEASES: DIAGNOSIS AND TREATMENT. By WILLIAM S. COLLENS, B. S., M. D., Metabolist, Chief of the Clinic for Peripheral Vascular Disease, Chief of the Diabetic Clinic, Israel Zion Hospital, Brooklyn; Associate Visiting Physician, Greenpoint Hospital; Metabolist, Jewish Sanitarium and Hospital for Chronic Diseases, etc.; and NATHAN D. WILENSKY, M. D., Assistant in Clinic for Peripheral Vascular Disease, Assistant in Diabetic Clinic, Israel Zion Hospital; Assistant Visiting Physician, Kings County Hospital. 243 pages, with 77 illustrations. Price, \$4.50. Springfield: Charles C Thomas, Publisher, 1939.

Arteriosclerosis is so common that it must involve the interests of every one practicing medicine. Other types of arterial disease are fortunately rather rare, yet they have attracted an enormous amount of research, both experimental and clinical, in recent years; indeed they have been recently ruled off in some quarters as a new superspecialty. It becomes us all therefore to know something about them. The authors of this book have conveniently supplied this knowledge in compact form to serve as a ready reference for the practitioner. The work is comprehensive and authoritative. One notes with pleasure that they do not lose sight of the importance of studying the patient as a whole even when vascular disease is evident. That they highly recommend Bourbon or Scotch (in small doses of course) in the treatment of arterial disease strikes a responsive chord in the heart of the reviewer.

One wonders why the book was not entitled "Peripheral Arterial Diseases." One wonders too if they may not be unduly enthusiastic over their own pet method of treatment, intermittent venous occlusion. At the same time, be it noted that all the other recognized modes of therapy are described.

THE PATIENT'S DILEMMA. THE QUEST FOR MEDICAL SECURITY IN AMERICA. By HUGH CABOT, M. D. 284 pages. Price, \$2.50. New York: Reynal & Hitchcock, 1940.

The more conservative members of the medical profession believe that the American people today are receiving on the whole the best medical care that any people ever have received so far: that it is good enough. This belief has been noisily combated in the last ten years and we have been inundated with discussions of the "problem" of "adequate medical care."

Let us strip this problem of its non-essentials: the people at large don't give a continental whether we of the medical profession are prosperous and happy or not; they don't even care whether we are contented. If they become convinced that they are not now getting "good medical care," they will demand it regardless. We are not sacrosanct, we cannot say with the railroad tycoon of another day, "The public be damned." If radical changes in the present system of medical practice in this country will provide better medical service to the public, we not only must but should reconcile ourselves to it. On the other hand, if the present system is fundamentally right, we should do our best to perfect it, and we must also convince the people at large that radical changes are dangerous to *them*. To discuss the problem intelligently we must learn the side of those who disagree with us, and it would be difficult to learn this in a more agreeable way than by a perusal of "The Patient's Dilemma."

Dr. Cabot's latest opus is highly readable, seasoned with a sprightly humor and innumerable split infinitives. His solution of the problem of "good medical care" will run counter to the sentiments of most doctors, including this one. While he may be a prophet crying in the wilderness, he may be merely an ill bird.

A MANUAL FOR DIABETIC PATIENTS. By W. D. SANSUM, M. D., Chief of Staff of The Sansum Clinic and Director of Metabolic Research of the Santa Barbara Cottage Hospital; ALFRED E. KOEHLER, PH. D., M. D., and RUTH BOWDEN, B. S. 227 pages, with 11 illustrations. Price, \$3.25. New York: The MacMillan Company, 1939.

The surgeon will be safe in recommending this manual to his diabetic patients. It was Dr. Sansum, by the way, who some years ago at the risk of excommunication first insisted a diabetic patient must have a fair amount of carbohydrate: he must have enjoyed seeing the medical world come around to his way of thinking.

HARVEY CUSHING'S SEVENTIETH BIRTHDAY PARTY, APRIL 8, 1939. SPEECHES, LETTERS, TRIBUTES. 146 pages, with 10 illustrations. Price, \$3. Published for The Harvey Cushing Society. Springfield and Baltimore: Charles C Thomas, Publisher, 1939.

It is fortunate indeed that flowers were given Dr. Cushing before his death: his admirers whose name is legion will cherish this collection of them.

THE NEUROGENIC BLADDER. By FREDERICK C. McLELLAN, M. S., M. D., Instructor in Surgery, University of Michigan Medical School, Ann Arbor, Michigan. 206 pages, with 8 figures and 49 charts. Price, \$4. Springfield and Baltimore: Charles C Thomas, Publisher, 1939.

The "cord bladder" of *tabes dorsalis* is familiar to all of us: that is to say, we all know that in advanced *tabes* the patient has difficulty in emptying his bladder. But it is to be feared that is about as far as the knowledge—or the interest—of many of us extends. It will come as a surprise therefore to see a book devoted to the neurologic disorders of the bladder.

This volume is a young masterpiece. It takes up the normal bladder, the neurologic anatomy, the physiology of the autonomic nervous system, the neurophysiology of the bladder. Considerable space is devoted to cystometry. The chapter on treatment gives all that is now known, though it must be admitted that even the best treatment does not always give brilliant results. The appendix tabulates 100 cases of neurogenic bladder, with charts on a good many of them.

Incidentally the book is also a typographical masterpiece.

PROCTOSCOPIC EXAMINATION AND DIAGNOSIS AND TREATMENT OF DIARRHEAS. By M. H. STREICHER, M. S., M. D., University of Illinois, College of Medicine; Research and Educational Hospital, and Grant Hospital of Chicago. 149 pages, with 39 illustrations. Price, \$3. Springfield and Baltimore: Charles C Thomas, Publisher, 1939.

This book is noteworthy chiefly for its insistence on the importance of proctoscopic examination. In spite of Osler's insistence on the necessity for examining carefully all the body orifices (how greatly the instruments for

such examinations have been improved since his day!) it is to be feared that even today the examiner's finger does not always penetrate the anal sphincter. Diagnosis should be improved with routine proctoscopic inspection.

Diarrhea is one of the most annoying symptoms. Its causes are manifold: the successful treatment of any case demands first the discovery of its cause. This little volume will facilitate that discovery and it outlines the accepted treatment: it should therefore prove popular.

A HANDBOOK OF ELEMENTARY PSYCHOBIOLOGY AND PSYCHIATRY. By EDWARD G. BILLINGS, B. S., M. D., M. D. Cum Laude (Ind.), Assistant Professor of Psychiatry, University of Colorado School of Medicine, etc., etc. 271 pages. Price, \$2. New York: The Macmillan Company, 1939.

The day (if there ever was such a day) when the surgeon could be content with his skill in wielding a scalpel has passed but definitely. He must often have an understanding of his patient's personal problems to avoid the unnecessary removal of organs. Dr. Billings' pocket size book will prove a help to his gaining such an understanding,—particularly since it is not written in a psychiatrist's individually invented neo-Greek.

OFFICE GYNECOLOGY. By J. P. GREENHILL, B.S., M.D., F.A.C.S., Professor of Obstetrics and Gynecology, Loyola University Medical School, Chicago; Professor of Gynecology, Cook County Graduate School of Medicine; Attending Gynecologist, Cook County Hospital; Editor of "Gynecology" in the *Year Book of Obstetrics & Gynecology*; Author of *Obstetrics for the General Practitioner*. 406 pages, with 106 illustrations. Chicago: The Year Book Publishers, Inc., 1939.

This book starts with pointers on taking the history of gynecologic patients and examining them. Some of these may be unknown to the young man who is just beginning to work in his own office, no matter how fine his hospital training. It's better for him to learn them from this book than by the hard way. Other chapters concern, among other subjects, trichomoniasis, gonorrhea, dyspareunia, sterility, control of conception, artificial insemination, anorectal diseases, obesity and premarital interviews. Particularly would we recommend the longest chapter in the book, that on endocrinology. Dr. Greenhill does not claim the impossible for hormone therapy (nor does he blame obesity on endocrine dysfunction; he says it is almost always due to over-eating, praise Allah). Considerately for those of us who tend to get confused among all the proprietary names of commercial preparations, he lists, for example, twelve terms for estrogenic substance prepared by as many manufacturers: it goes without saying he specifies only dependable products of reliable concerns—all of whom should advertise in *THE SOUTHERN SURGEON* (though only Ciba does so regularly).

In some respects this book may appear elementary, in others it may seem rather advanced. On the whole however, it is well written, clear, concise, authoritative. The gynecologist who regularly attends conventions of his peers and keeps abreast of the current literature will find little use for this work; other doctors should find it often most useful.

THE ESSENTIALS OF APPLIED MEDICAL LABORATORY TECHNIC. *Details of How to Build and Conduct a Laboratory in Hospital or Office at Small Cost.* By J. M. FEDER, M.D., Director of Laboratories and Allergic Service, Anderson County Hospital, Anderson, S. C. 234 pages, profusely illustrated; two plates in colors. Price, \$5. Charlotte, N. C.: Charlotte Medical Press, 1940.

Dr. Feder feels that, though there exists a "plethora of Laboratory Manuals and books on Clinical Pathology," these books "presuppose more knowledge of the fundamental sciences involved" than can be expected from the technician in a small hospital or the average doctor's office assistant. He thinks also that such books usually assume too expensive equipment or else do not go into detail with regard to enough tests. He has therefore attempted to prepare a book that will meet the needs of a small hospital or of the doctor who has not ready access to a big laboratory. In the opinion of this reviewer, he has succeeded admirably.

To begin with, he describes in detail the equipment necessary for routine tests. Not including the microscope he estimates that this can be installed for about \$200. (One suspects he does include metabolism determinations under routine tests, and he does not mention roentgenology or electrocardiography.) The laboratory table, shelves, etc., he describes in sufficient detail to be made by a local carpenter and they appear to be models of efficiency. He suggests many things that can be bought from a hardware store will serve every purpose as well as those many times as expensive from a surgical supply house. Occasionally he cites the company that makes economically the apparatus he has found satisfactory.

Modestly Dr. Feder does not claim that any procedure he describes as his own, but one suspects that some of them he originated and many more he has modified. Every examination is described simply and clearly and, so far as this reviewer is able to judge, should give dependable results. It is up to date enough to include determinations of sulfanilamide concentration in the blood.

One feels that a careful study of this book should enable the chief of laboratory in a medical school or large hospital to effect many economies and at the same time that the book is essential for the smaller institution. Now that hospitals are springing up in so many small towns, it should have a wide sphere of usefulness.

One cannot close the discussion of Dr. Feder's manual without saying that he evidently speaks from extensive first hand experience, which has included the necessity for making each dollar go just as far as possible; that he writes in a warm, friendly way and that he has not prepared a book on clinical medicine; he evidently believes the laboratory worker should do her job and allow the physician to draw his own conclusions from her reports.

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